MULTIPLE MYELOMA Research Foundation

Opening Remarks

Mary DeRome, MS
MMRF

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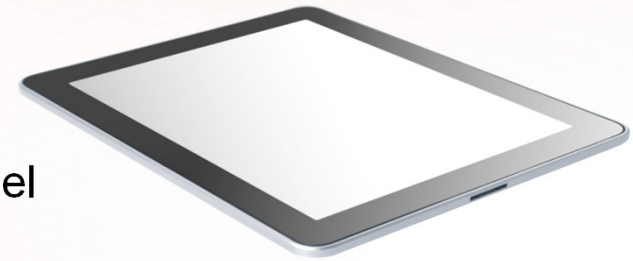
  - Take notes
  - Submit questions to panel
  - Program evaluation



Throughout the Summit, use the same e-mail address to log on to any iPad.

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Program Faculty

Program Host

Laura Finn, MD, MS
Ochsner Health
New Orleans, Louisiana

Faculty

Ambuga R. Badari, MD
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City of Hope Medical Center
Duarte, California

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Toronto, Ontario, Canada

Paul G. Richardson, MD
Dana-Farber Cancer Institute
Boston, Massachusetts

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Summit Agenda

Time (ET)	Topic	Speakers
12:00 – 12:15 PM	Introduction to the MMRF	Mary DeRome, MS
12:15 – 12:25 PM	Welcome	Laura Finn, MD, MS
12:25 – 12:55 PM	Myeloma 101	A. Keith Stewart, MBChB
12:55 – 1:25 PM	MGUS/SMM	Ambuga R. Badari, MD
1:25 – 1:55 PM	Town Hall Q&A	Panel
1:55 – 2:25 PM	Newly Diagnosed Multiple Myeloma	Amrita Y. Krishnan, MD, FACP
2:25 – 2:55 PM	Relapsed/Refractory MM and Treatments on the Horizon	Paul G. Richardson, MD
2:55 – 3:25 PM	Health Care Disparities in MM	Laura Finn, MD, MS Yvens Laborde, MD
3:25 – 3:40 PM	Break	
3:40 – 3:55 PM	Patient Journey	
3:55 – 4:25 PM	Town Hall Q&A	Panel
4:25 PM	Closing Remarks	Mary DeRome, MS

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MULTIPLE MYELOMA Research Foundation

MMRF Introduction

Mary DeRome, MS
MMRF

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The Work of the MMRF

The MMRF does three things in relentless pursuit of its mission to accelerate a cure for each and every myeloma patient.

1

We accelerate new treatments

Bringing next-generation therapies to patients faster

2

We drive precision medicine

Using data to deliver better answers and more precise treatments for patients

3

We empower patients

Putting them on The Right Track and guiding them to the right team, tests, and treatments to extend their lives

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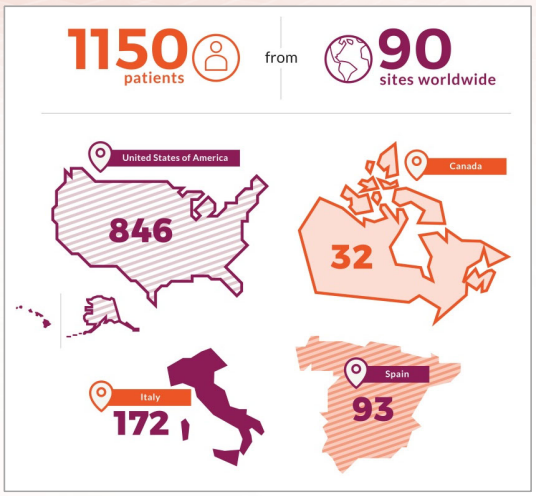
MMRF CoMMpass Study: Advancing Personalized Medicine Research

- Landmark study focusing on the genomics of myeloma
- Goals
  - Learn which patients respond best to which therapies
  - Identify new targets and new hypotheses
- Newly diagnosed patients will be followed for at least 8 years

All participants undergo a type of detailed genetic testing called *genomic sequencing.*



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CoMMpass Is a Trial of Discovery

- CoMMpass data has
  - Provided the myeloma community with information on
    - Frequency of genetic abnormalities
    - How genetic abnormalities play a role in myeloma
      - Drive multiple myeloma cell growth and survival
      - Contribute to drug resistance
      - May predict which patients respond to which therapy
    - Genetic abnormalities that help refine risk assessment
  - Led to conception of the MyDRUG trial

All patients in CoMMpass had genomic sequencing from diagnosis to relapse. The resulting data provides detailed genetic profiles for every myeloma patient at every stage of their disease!

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The MMRF CureCloud®: a 5000-patient research study

MMRF CureCloud®

Together, we can make a difference for every patient with multiple myeloma.

We are making progress in the fight against myeloma because of contributions from patients like you.
People with multiple myeloma are living longer than ever before — but there's still no cure for most patients. Medical advances have been possible because patients have participated in clinical studies.

The MMRF CureCloud® study aims to identify more personalized treatments for every myeloma patient, faster.
The fastest way to find these treatments is to make information from every myeloma patient available to cancer researchers.

Myeloma is different in every patient — we need to learn more to see what's best for each patient.

It's easy and convenient to participate from home — at no cost to you or your doctor.

Unlike other studies, in the CureCloud you will not need to:
- ✖ Take any experimental medication or change your current medications.
- ✖ Go for any extra doctor's visits or see a different doctor.

Sign up online or in a CureCloud participating clinic and confirm your eligibility.
- ✔ Get a home blood test (genomic test*).
- ✔ We'll collect your medical records.

You'll help researchers find better treatments while learning more about your myeloma.
Information contributed by you and other patients will help researchers find better therapies for every myeloma patient, faster. We'll share with you anything we find out about your myeloma from your blood test and medical records.

Your data is strictly protected — the information you provide is held in a very secure database.

**Genomic test: analysis of myeloma DNA in your blood to see if there are any changes.*

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How does the MMRF CureCloud work?

You'll get a blood test at home.

- After you sign up, you will receive a CureCloud bloodwork kit..
- A trained medical professional will come to your home to draw your blood.

We'll collect your medical records.

- When you sign up, you'll provide the names and contact information for the doctors who have treated your myeloma and any clinics or hospitals where you've had tests (bone scans, MRI, etc.).
- We'll contact them and collect your records.

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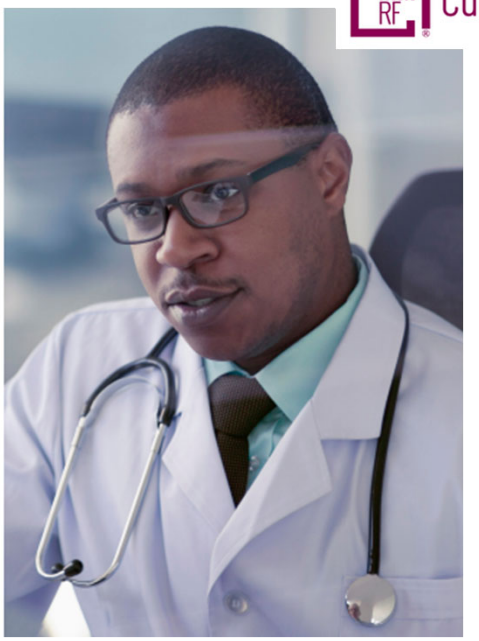
What happens to my information?

Your information is shared anonymously — to help the entire myeloma community.
The information you contribute is made anonymous and will be available to the myeloma community. Researchers will be able to use this information to learn more about myeloma, helping to find new medicines or even, someday, a cure. In the future, patients and their doctors will be able to access this data to find specific treatment options that are right for them.

You'll learn more about *your* myeloma.
Once we've collected your medical records, you'll have access to a private, personal dashboard with all the medical information related to your myeloma*.

With all your information at hand, you'll be able to have better conversations with your myeloma care team.

**Information will only be collected from the myeloma doctors you provide when you sign up.*



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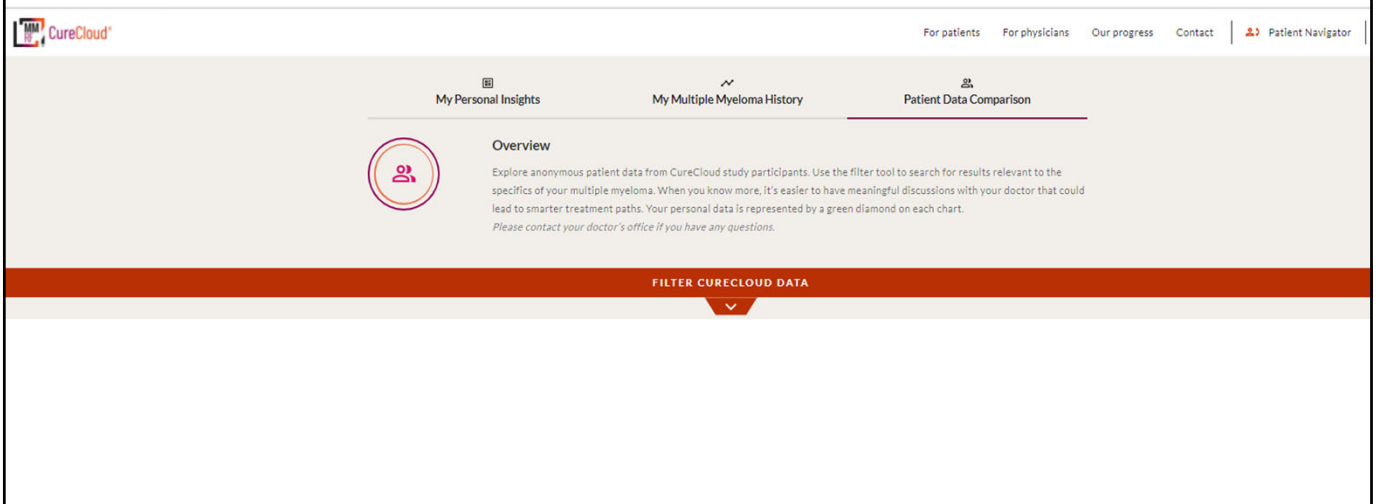
CureCloud®



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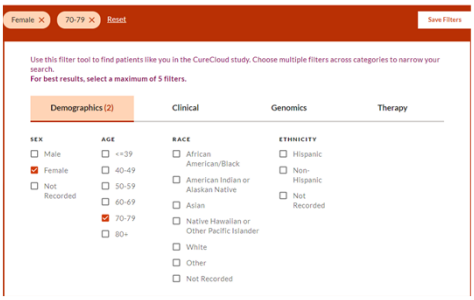
A Patient's Own Data–Compared With Data From Many Others

- Clinical data with patient's data represented (green diamond)
- Patient can filter data by characteristics like age, sex, and race to see patients like themselves



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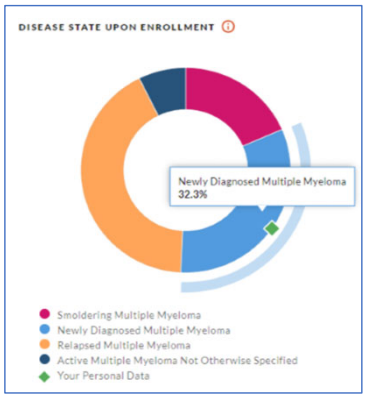

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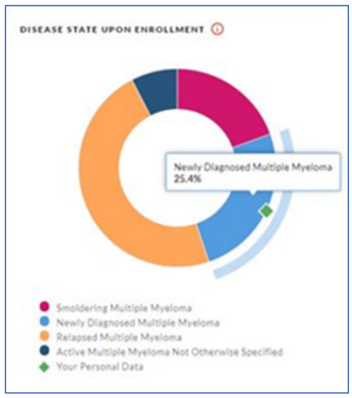

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A Patient's Own Data–Compared With Data From Many Others

- Clinical data with patient's data represented (green diamond)
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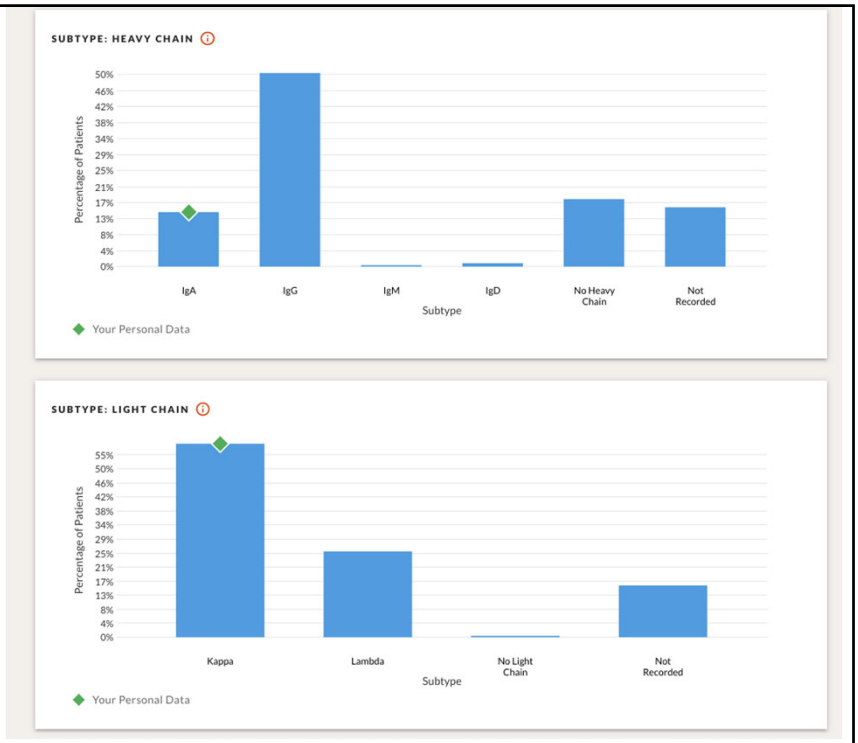
CureCloud®



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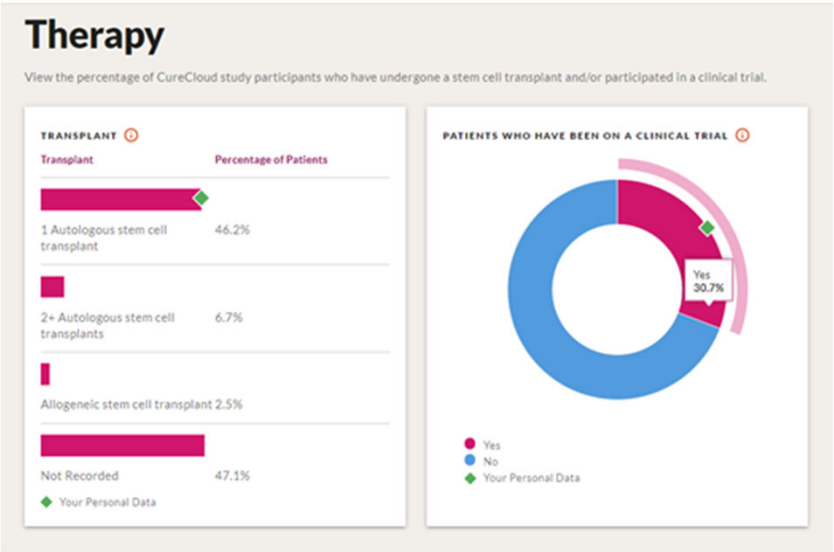
A Patient's Own Data–Compared With Data From Many Others

- Treatment data with patient's data represented (green diamond)
- Patient can filter data by characteristics like age, sex, and race to see patients like themselves

CureCloud®



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Thank you

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Welcome!

Laura Finn, MD, MS
Ochsner Health
New Orleans, Louisiana

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Question

Are you a...

A. Patient
B. Caregiver (family member or friend who helps patient manage his or her disease)
C. Other

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Question

At what stage is your myeloma? (If you are a caregiver, what is the stage of the patient's myeloma?)

A. Newly diagnosed
B. Relapsed/refractory
C. Remission: still on therapy
D. Remission: not on therapy
E. MGUS or smoldering myeloma not currently requiring treatment
F. Other
G. I don't know.

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Question

Have you had a stem cell transplant?

A. No, but I will soon!
B. No, but I am considering one (or my doctor is discussing with me).
C. No, my doctor tells me I am not a candidate.
D. Yes
E. Not applicable

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Question

Do you know if you had any molecular characterization performed on your tumor, such as FISH, cytogenetics, or sequencing?

A. No
B. Yes, I had FISH.
C. Yes, I had cytogenetics.
D. Yes, I had sequencing.
E. Yes, I had more than one of these tests performed.
F. I don't know.

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Question

Have you and your care team ever discussed the possibility of you joining a clinical trial that you are eligible for? (If you are a caregiver, do you know if joining a clinical trial has ever been discussed?)

A. Yes

B. No

C. I don't know.

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Myeloma 101

A. Keith Stewart MBChB
Princess Margaret Cancer Centre
Toronto, Ontario, Canada

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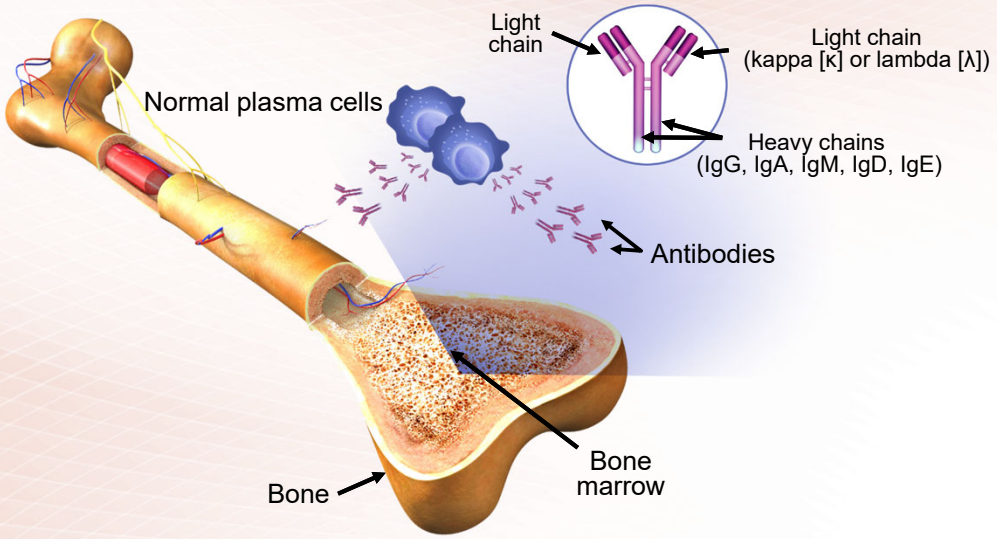
Normal Bone Marrow



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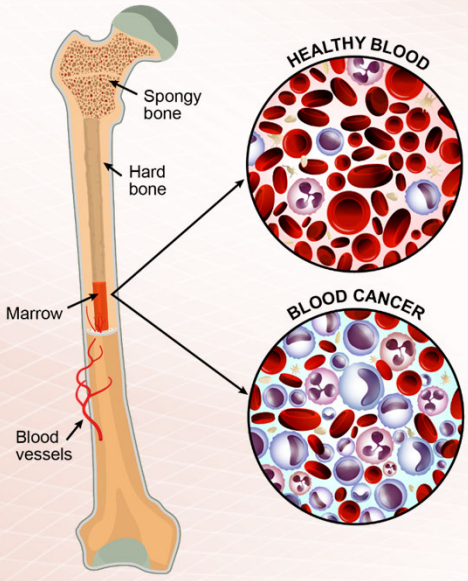
What is multiple myeloma?



- Multiple myeloma is a **blood cancer** that starts in the **bone marrow**, the place where all **blood cells** are produced
- Multiple myeloma is caused when a type of **white blood cell** called a **plasma cell** becomes cancerous and grows out of control

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Demographic Risk Factors: Multiple Myeloma

- Older age
- Male sex
- Obesity
- Race
  - ↑ Blacks (2× Whites)
  - Ashkenazi Jews
  - Europe: Ireland
  - ↓ Asian

Family history risks

One first-degree relative with multiple myeloma

Relatives of multiple myeloma patients have more monoclonal gammopathy of undetermined significance (MGUS)

Schinasi LH et al. *Br J Haematol*. 2016;175:87.
Thordardottir M et al. *Blood Adv*. 2017;1:2186.

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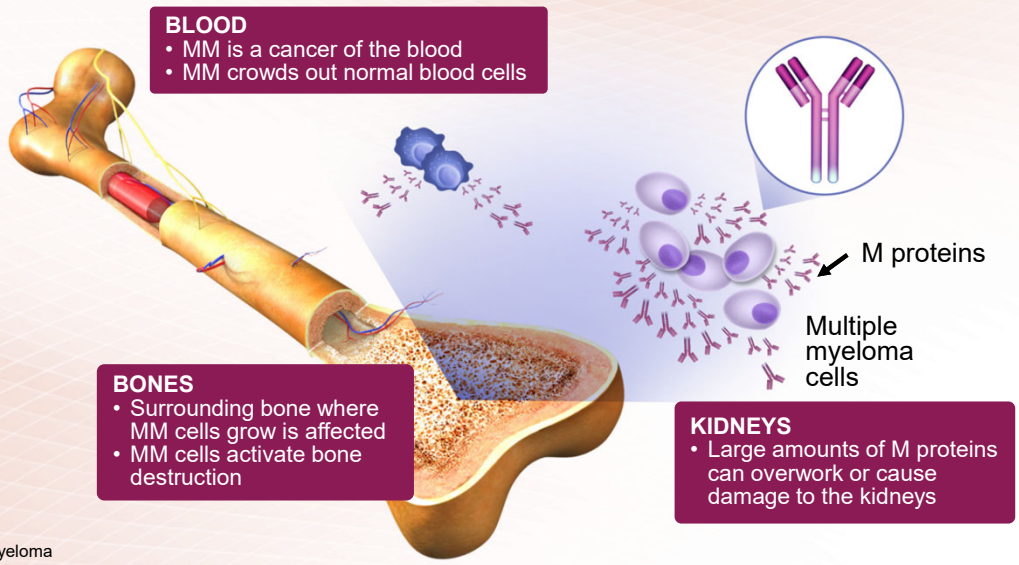
Multiple Myeloma Affects Your Bones, Blood, and Kidneys



MM, multiple myeloma

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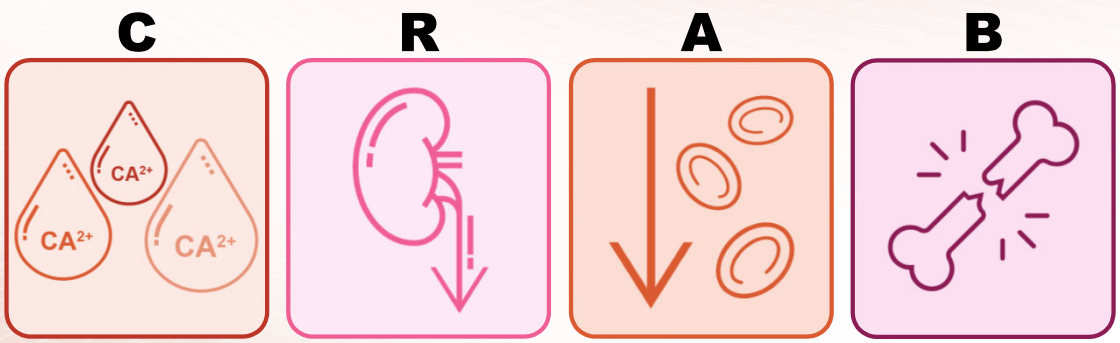
Multiple Myeloma Affects Your Bones, Blood, and Kidneys

The clinical features that are characteristic of multiple myeloma



C	R	A	B
High levels of **c**alcium in the blood	Decreased kidney (**r**enal) function	Low amount of red blood cells (**a**nemia)	Presence of **b**one damage

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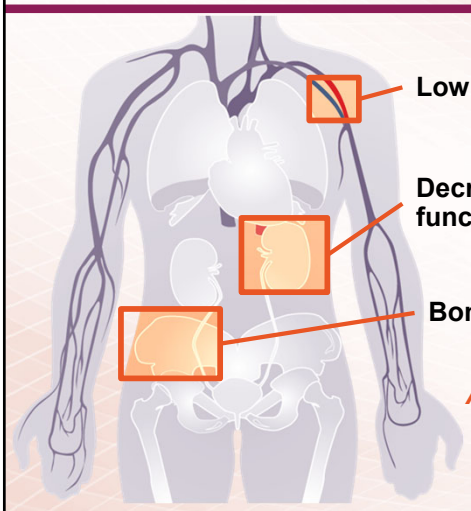
Effects of Myeloma and Common Symptoms



- **Low blood counts** → **Weakness, Fatigue, Infection**
- **Decreased kidney function** → **Weakness**
- **Bone damage** → **Bone pain**

About 10% to 20% of patients with newly diagnosed myeloma do not have any symptoms.

Disease presentation and myeloma-related complications after myeloma diagnosis are different in patients by race

More common in Black patients

- Hypercalcemia
- Kidney dysfunction
  - Hemodialysis
- Anemia

Less common in Black patients

- Bone fractures

MMRF. Multiple myeloma symptoms, side effects, and complications. https://themmrf.org/multiple-myeloma/symptoms-side-effects-and-complications/.
Campbell K. *Nurs Times*. 2014;110:12; Kyle R et al. *Mayo Clin Proc*. 2003;78:21; Ailawadhi S et al. *Cancer*. 2018;124:1710.

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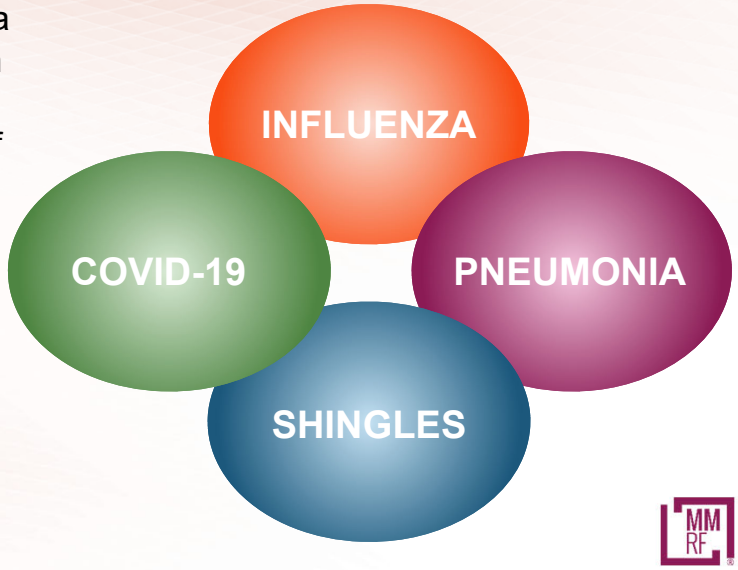
Infections and Vaccinations in Multiple Myeloma

- Risk of infection higher for myeloma patients than for general population
- Types of infections include
  - Bacterial: pneumonia (an infection of the lungs), bacteremia
  - Viral: varicella zoster (shingles), influenza, COVID
- Preventive strategies (prophylaxis) are recommended
  - Hand-washing, avoiding sick contacts
  - Vaccines/pre-exposure antibodies
  - Other precautions (antibiotics, growth factors)



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Following the Proper Path Will Help Patients Get the Best Treatment and Results for Their Specific Type of Myeloma

Right Team

Access experts and centers that have extensive experience treating multiple myeloma

Right Tests

Get the information, tests and precise diagnoses to make the right treatment decisions

Right Treatment

Work with your team to decide on the best treatment plan and identify clinical trials that are right for you

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The Right Team

Connect with a myeloma specialist—a doctor who diagnoses and treats a high number of myeloma patients

Seek a second opinion at any point in your journey

Available resources

MMRF's online myeloma treatment locator: **themmrf.org/resources/find-a-treatment-center**

Contact the MMRF Patient Navigation Center: **themmrf.org/resources/patient-navigation-center**

1-888-841-MMRF (6673)

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The Right Tests

Common laboratory tests conducted

Blood tests

- Complete blood count (CBC)
- Complete metabolic panel (CMP)
- Chemistries
  - Calcium
  - Creatinine
  - Lactate dehydrogenase (LDH)
  - Beta-2 microglobulin
- **Serum protein electrophoresis (SPEP) with immunofixation electrophoresis (IFE)**
- **Serum free light chain assay (SFLC)**

Confirms the type of myeloma

Urine tests

- Urine protein electrophoresis (UPEP) with IFE
- 24-hour urine

Bone marrow biopsy

Conventional
- **Fluorescence in situ hybridization (FISH)**

New
- Genomic sequencing

Determines how advanced the myeloma is and identifies the myeloma subtype

Imaging tests

- X-ray
- **MRI**
- **Whole-body, low-dose CT scan**
- **PET scan**
- Metastatic bone survey

Assess changes in the bone structure and determine the number and size of tumors in the bone

Detects the extent of bone disease and the presence of myeloma outside of the bone marrow

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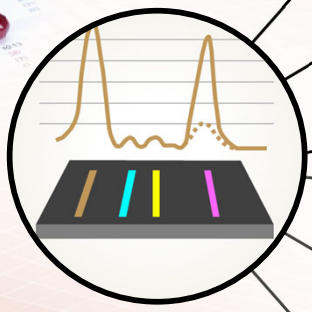
Learn Your Labs!
Blood Tests

Blood tests



- **CBC** — Number of red blood cells, white blood cells, and platelets
- **CMP** — Measure levels of albumin, calcium, lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and creatinine. Assess function of kidney, liver, and bone status and the extent of disease
- **B2M** — Determine the level of a protein that indicates the presence/extent of MM and kidney function
- **SPEP** — **Detect the presence and level of M protein**
- **IFE** — **Identify the type of abnormal antibody proteins**
- **SFLC** — **Freelite test measures light chains (kappa or lambda)**

CBC, complete blood count; CMP, complete metabolic panel; B2M; beta-2 microglobulin; SPEP, serum protein electrophoresis; IFE, immunofixation electrophoresis; SFLC, serum free light chain assay

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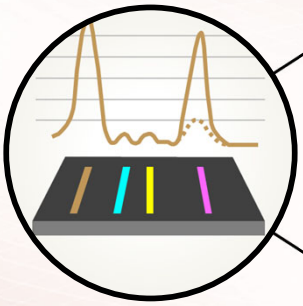
Learn Your Labs!
Urine Tests

Urine tests



- **UPEP** — Detect Bence Jones proteins (otherwise known as myeloma light chains)
- **24-hr urine analysis** — Determine the presence and levels of M protein and Bence Jones protein

UPEP, urine protein electrophoresis

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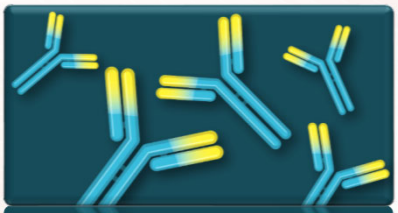
Types of Multiple Myeloma Based on Blood or Urine Tests



Intact M protein

- Named for the type of immunoglobulin and light chain pair; for example, IgG kappa (κ) or IgG lambda (λ)

80%

Light chain only

- Also known as Bence Jones protein
- Renal failure more common in light chain multiple myeloma

20%

Non-secretory

- No M protein present

3%

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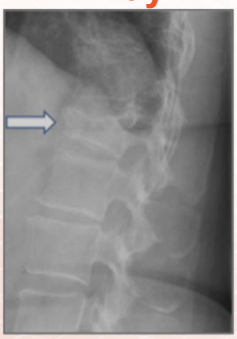
Know Your Imaging Tests!

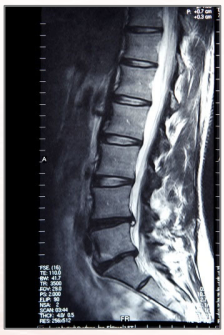
Assess changes in the bone structure and determine the number and size of tumors in the bone

X-ray

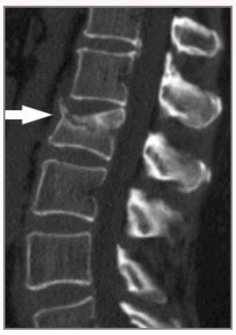


Conventional x-rays reveal punched-out lytic lesions, osteoporosis, or fractures in 75% of patients.

MRI



CT scan



PET scan

MRI and PET/CT appear to be more sensitive (85%) than skeletal x-rays for the detection of small lytic bone lesions.

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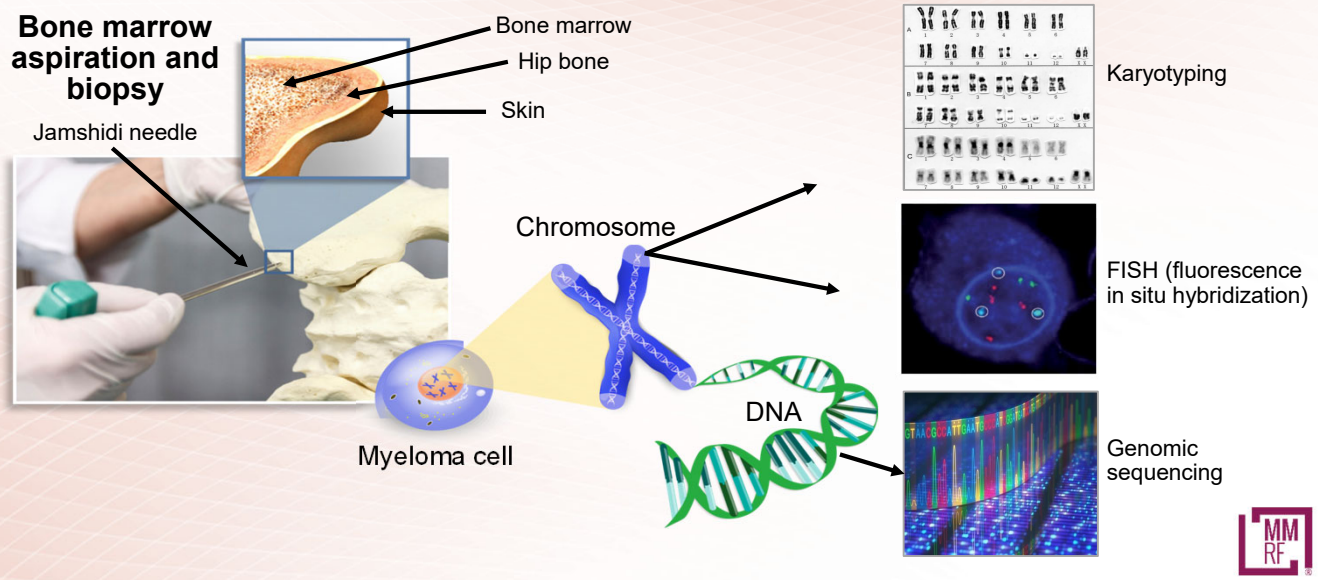
Know Your Bone Marrow Tests!



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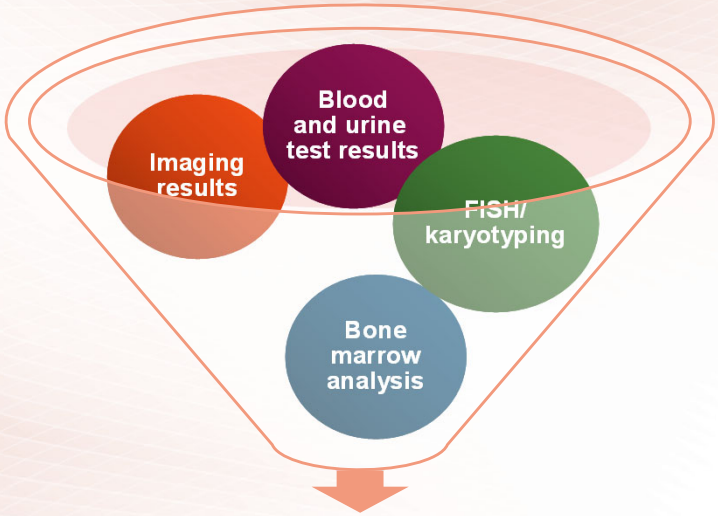
Putting the Results Together



Staging, prognosis, and risk assessment

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Multiple Myeloma Prognosis and Risk

Revised-International Staging System (R-ISS)

R-ISS stage	Laboratory measurements
I	• Serum β2M level <3.5 mg/L • Serum albumin level ≥3.5 g/dL • No high-risk CA* • Normal LDH level
II	All other possible combinations
III	• Serum β2M level ≥5.5 mg/L • High-risk CA* or high LDH level

*High-risk chromosomal abnormality (CA) by FISH: del(17p) and/or t(4;14) and/or t(14;16)

Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines

High risk
- High-risk genetic abnormalities
  - t(4;14)
  - t(14;16)
  - t(14;20)
  - Del 17p
  - p53 mutation
  - Gain 1q
- RISS Stage 3
- High plasma cell S-phase
- GEP: high-risk signature

- *Double-hit myeloma*: any two high-risk genetic abnormalities
- *Triple-hit myeloma*: three or more high-risk genetic abnormalities

Standard risk
- All others including:
  - Trisomies
  - t(11;14)
  - t(6;14)

Currently cannot identify with great certainty all high-risk patients.

β2M; beta-2 microglobulin; LDH, lactate dehydrogenase

Greipp PR et al. *J Clin Oncol*. 2005;23:3412.; Palumbo A et al. *J Clin Oncol*. 2015;33:2863; Mikhael JR et al. *Mayo Clin Proc*. 2013;88:360.

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Multiple Myeloma Prognosis and Risk

Many blood test and bone marrow biopsy test results can determine a patient's risk for myeloma that is aggressive (high risk) or not (standard risk) based on the revised-International Staging System (R-ISS)

Standard risk

R-ISS Stage I

- Serum β2M level <3.5 mg/L
- Serum albumin level ≥3.5 g/dL
- No high-risk chromosomal abnormality*
- Normal LDH level

All other possible combinations of the test results means that a patient is **R-ISS stage II**

High risk

R-ISS Stage III

- Serum β2M level ≥5.5 mg/L
- High-risk chromosomal abnormality* or high LDH level

*High-risk chromosomal abnormality by FISH: del(17p) and/or t(4;14) and/or t(14;16)

β2M; beta-2 microglobulin; LDH, lactate dehydrogenase; FISH, fluorescent in situ hybridization

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The Right Treatment

- Know the treatment options available to you based on your myeloma subtype at each stage of your disease.
- Be aware of the pros and cons of each option.
- Clearly communicate your treatment goals and concerns to the care team.
- Find clinical trials that are right for you.

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Getting the Right Treatment: Goals of Multiple Myeloma Therapy

- **Reduce the amount of M protein (as measured by serum protein electrophoresis) or light chains (as measured via the free light chain test) to the lowest level possible.**
- **Eliminate myeloma cells from the bone marrow (as measured via minimal residual disease [MRD] testing).**
- **Improve quality of life with as few treatment side effects as possible.**
- **Provide the longest possible period of response before first relapse.**
- **Prolong overall survival.**

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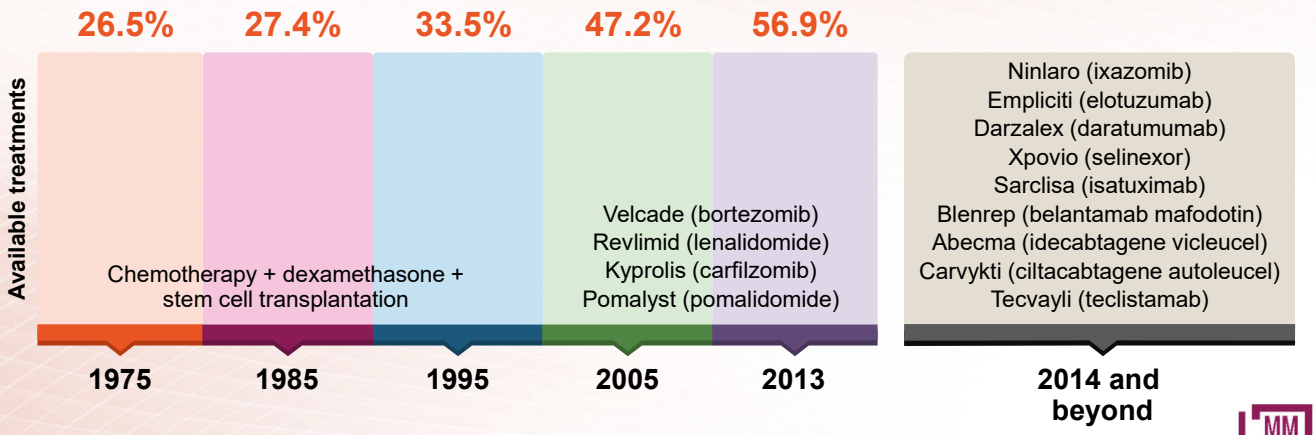
Myeloma Survival Has Improved Over Time Mainly Due to Current Drugs

The percentage of people expected to survive 5 years or more after being diagnosed with myeloma



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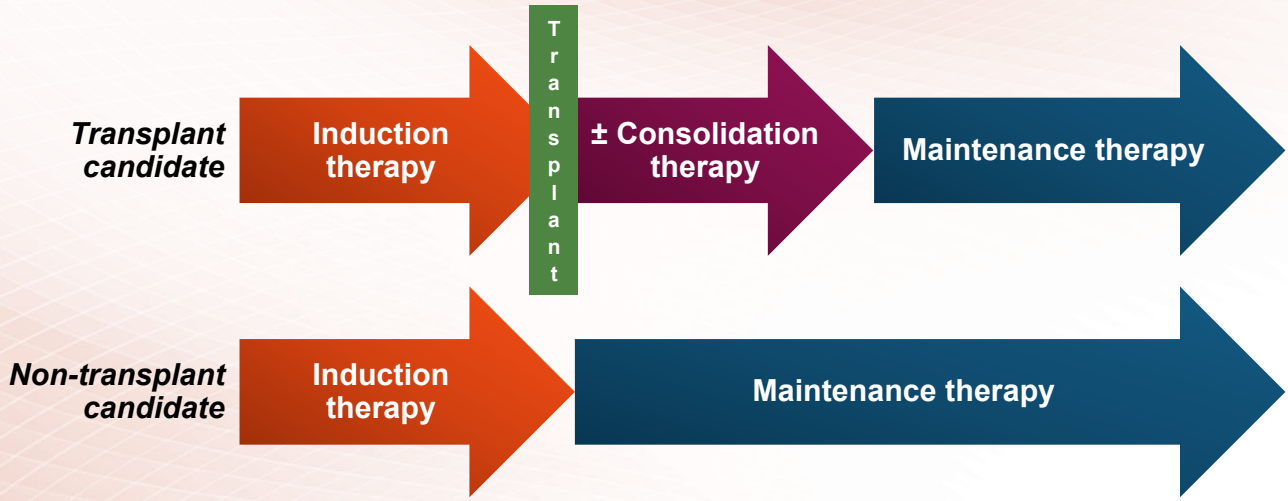
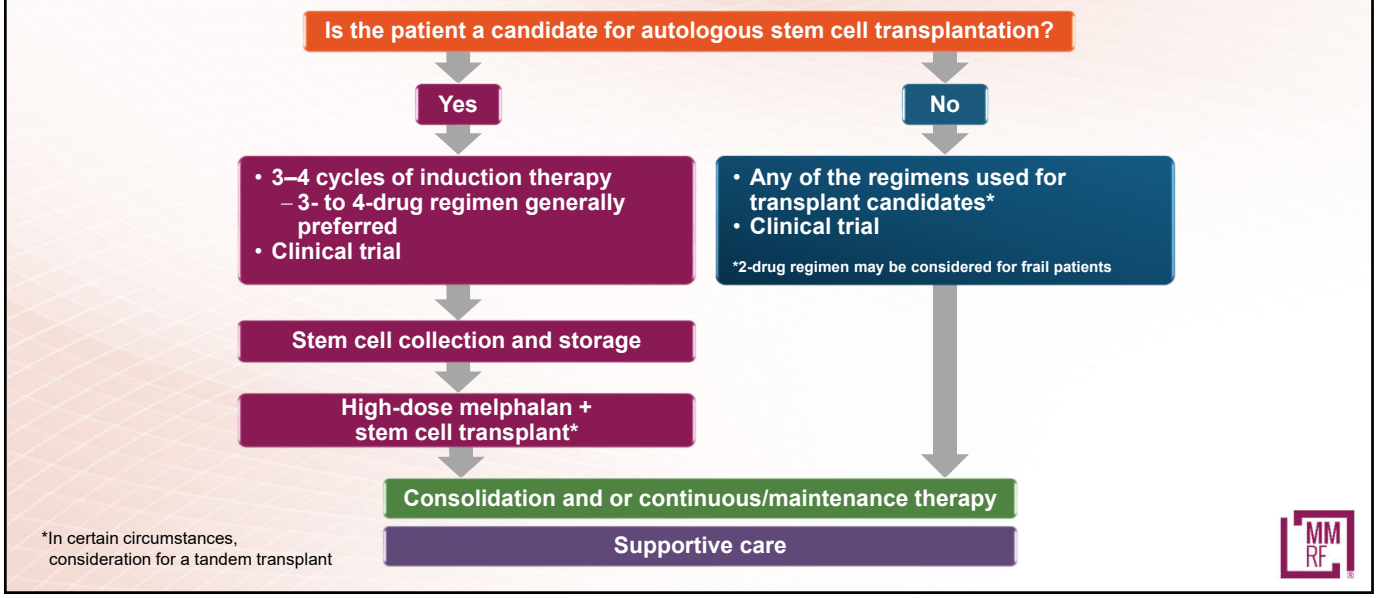
Current Treatment Paradigm for Newly Diagnosed Multiple Myeloma



46

Overview of Treatment Approach for Active Multiple Myeloma



*In certain circumstances, consideration for a tandem transplant

47

Induction Therapy Regimens

	Preferred	Recommended	Certain circumstances
Transplant eligible	• Revlimid-Velcade-dex (RVd)* • Revlimid-Kyprolis-dex	• Darzalex-Revlimid-Velcade-dex (D-RVd)	• Velcade-Thalomid-dex (VTd)* • Velcade-Cytoxan-dex (VCd) • Velcade-Doxil-dex (VDd) • Kyprolis-Cytoxan-dex (KCd) • Revlimid-Cytoxan-dex (RCd) • Darzalex-Velcade-Thalomid-dex (D-VTd) • Darzalex-Kyprolis-Revlimid-dex (D-KRd) • Darzalex-Cytoxan-Velcade-dex (D-VCd) • Ninlaro-Cytoxan-dex (ICd) • Ninlaro-Revlimid-dex • VTD-PACE
Transplant ineligible	• Revlimid-Velcade-dex (RVd)* • Darzalex-Revlimid-dex (DRd)*	• Darzalex-Velcade-melphalan-prednisone (D-VMP)* • Kyprolis-Revlimid-dex (KRd) • Darzalex-Cytoxan-Velcade-dex (D-VCd) • Ninlaro-Revlimid-dex (IRd)	• Revlimid-dex (Rd)* • Velcade-dex (Vd) • Velcade-Cytoxan-dex (VCd) • Revlimid-Velcade-dex (RVd)-lite • Kyprolis-Cytoxan-dex (KCd) • Revlimid-Cytoxan-dex (RCd)

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
National Comprehensive Cancer Network Guidelines Version 2.2023. Multiple Myeloma.

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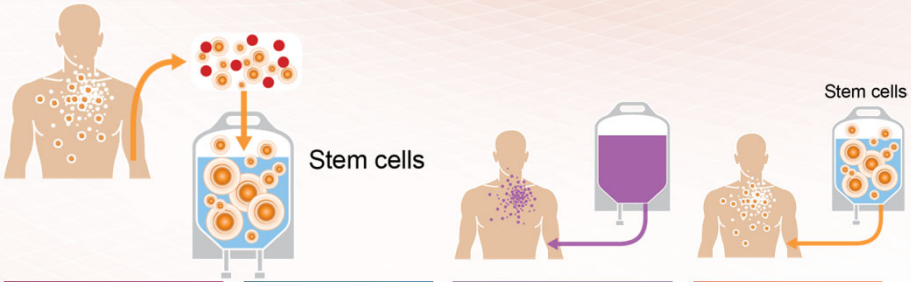
Autologous Stem Cell Transplantation



1. Induction therapy	2. Collection of stem cells from the bloodstream	3. Freezing of stem cells	4. High-dose chemotherapy	5. Thawing and infusion of stem cells	6. Recovery
~4–6 cycles	Stem cell mobilization • Neupogen, Neulasta, Leukine, Cytoxan, Mozobil	-2 to -3 weeks*	Melphalan • Alkeran, Evomela	Day 0	Days +1 to +100†

*The weeks leading up to the transplant; †The days after the transplant.

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Continuous or Maintenance Therapy Options

	Preferred	Recommended	Certain circumstances
Transplant eligible	• Revlimid*	• Velcade • Darzalex • Ninlaro	• Velcade-Revlimid ± dex • Kyprolis-Revlimid
Transplant ineligible	• Revlimid*	• Velcade • Ninlaro	• Velcade-Revlimid

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
National Comprehensive Cancer Network Guidelines Version 2.2023. Multiple Myeloma.

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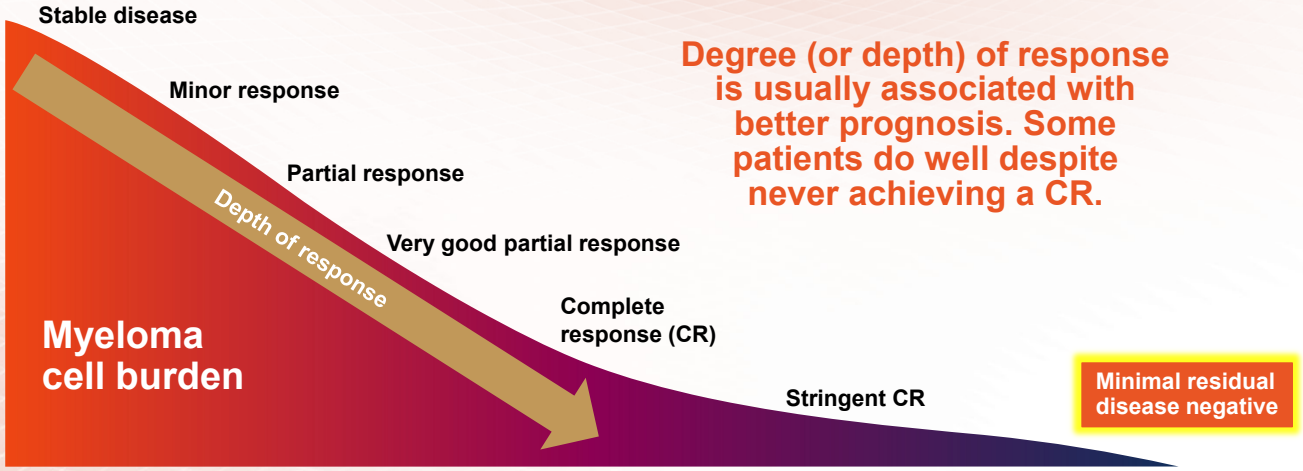
Measuring Response to Therapy



Degree (or depth) of response is usually associated with better prognosis. Some patients do well despite never achieving a CR.

ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients.

Palumbo A et al. *J Clin Oncol.* 2014;32:587.
Kumar S et al. *Lancet Oncol.* 2016;17:e328.

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Where is the myeloma field going?

- Staging with genomics and advanced imaging
- Higher efficacy using four-drug regimens
- Precision medicine and targeted therapies in subsets of patients—for example, t(11;14)
- MRD-driven therapy
- Minimize long-term toxicities since myeloma patients living (much) longer
- New drug classes and immunotherapies

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Summary

- Multiple myeloma is a rare blood cancer that can negatively affect the bones, kidneys, and the bone marrow, leading to lowered blood counts.
- The prognosis of multiple myeloma depends on the genetic makeup of myeloma cell chromosomes; R-ISS is used for staging in multiple myeloma.
- Survival rates are improving because of new drugs and new combinations of drugs.
- The treatment paradigm will continue to change with the approval of additional novel agents.
- Knowledge is power: right team, right test, right treatment.

Be an informed and empowered part of your health care team!

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Please take a moment to answer two questions about this presentation.

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MULTIPLE MYELOMA Research Foundation

Monoclonal Gammopathy of Undetermined Significance/ Smoldering Multiple Myeloma

Ambuga R. Badari, MD
Ochsner Health
New Orleans, Louisiana

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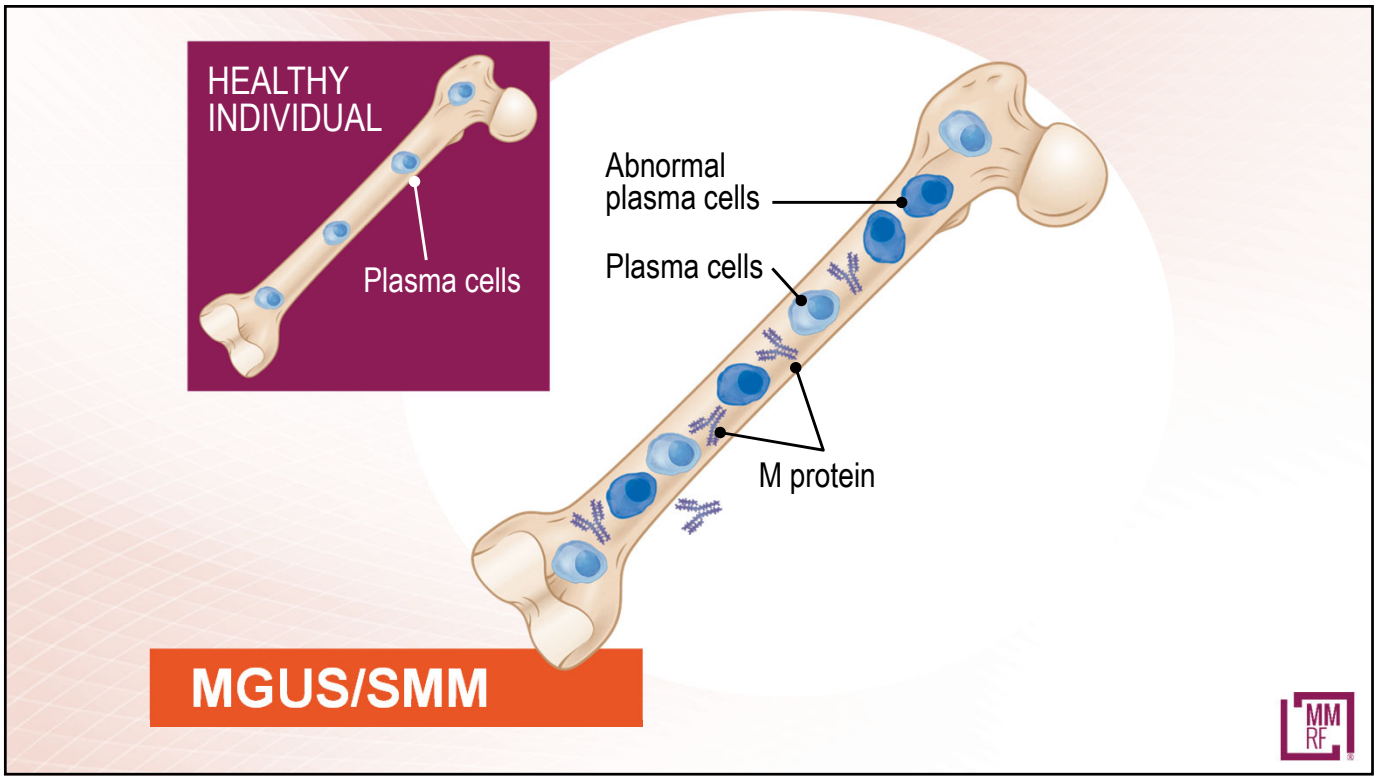

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Plasma Cell Disorders: Classification

Updated IMWG criteria for diagnosis of multiple myeloma

MGUS	Smoldering myeloma	Multiple myeloma
• M protein <3 g/dL • Clonal plasma cells in bone marrow <10% • No myeloma-defining events	• M protein ≥3 g/dL (serum) or ≥500 mg/24 hrs (urine) • Clonal plasma cells in bone marrow ≥10% to 60% • No myeloma-defining events	• Underlying plasma cell proliferative disorder **AND** • 1 or more myeloma-defining events • ≥1 CRAB* feature • Clonal plasma cells in bone marrow ≥60% • Serum free light chain ratio ≥100 • >1 MRI focal lesion

*C: Calcium elevation (>11 mg/dL or >1 mg/dL higher than ULN)
R: Renal insufficiency (creatinine clearance <40 mL/min or serum creatinine >2 mg/dL)
A: Anemia (Hb <10 g/dL or 2 g/dL < normal)
B: Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT)

Rajkumar SV et al. *Lancet Oncol.* 2014;15:e538.

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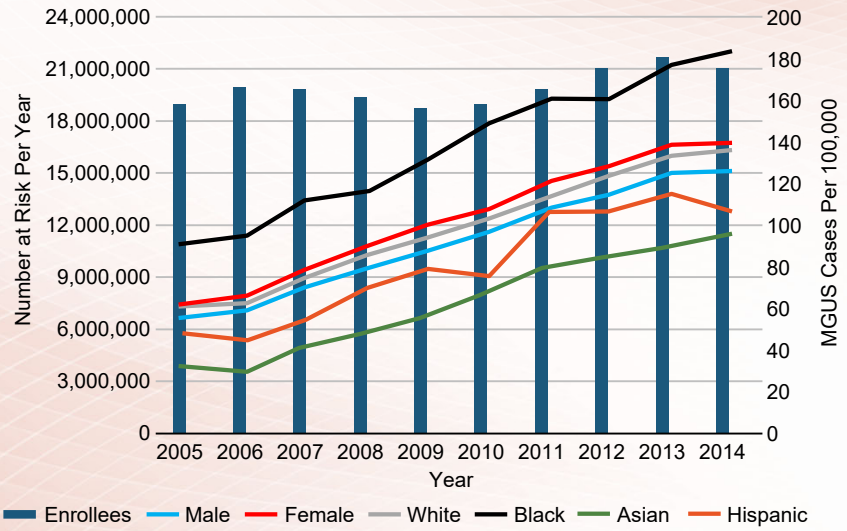
MGUS is a Very Common Condition



- 3% of the general population at age 50 has MGUS
- This rate is 3 times higher for individuals of African descent
- This rate is 2–3 times higher for first-degree family members of myeloma patients

Go RS et al. *Leukemia.* 2016;30:1443.

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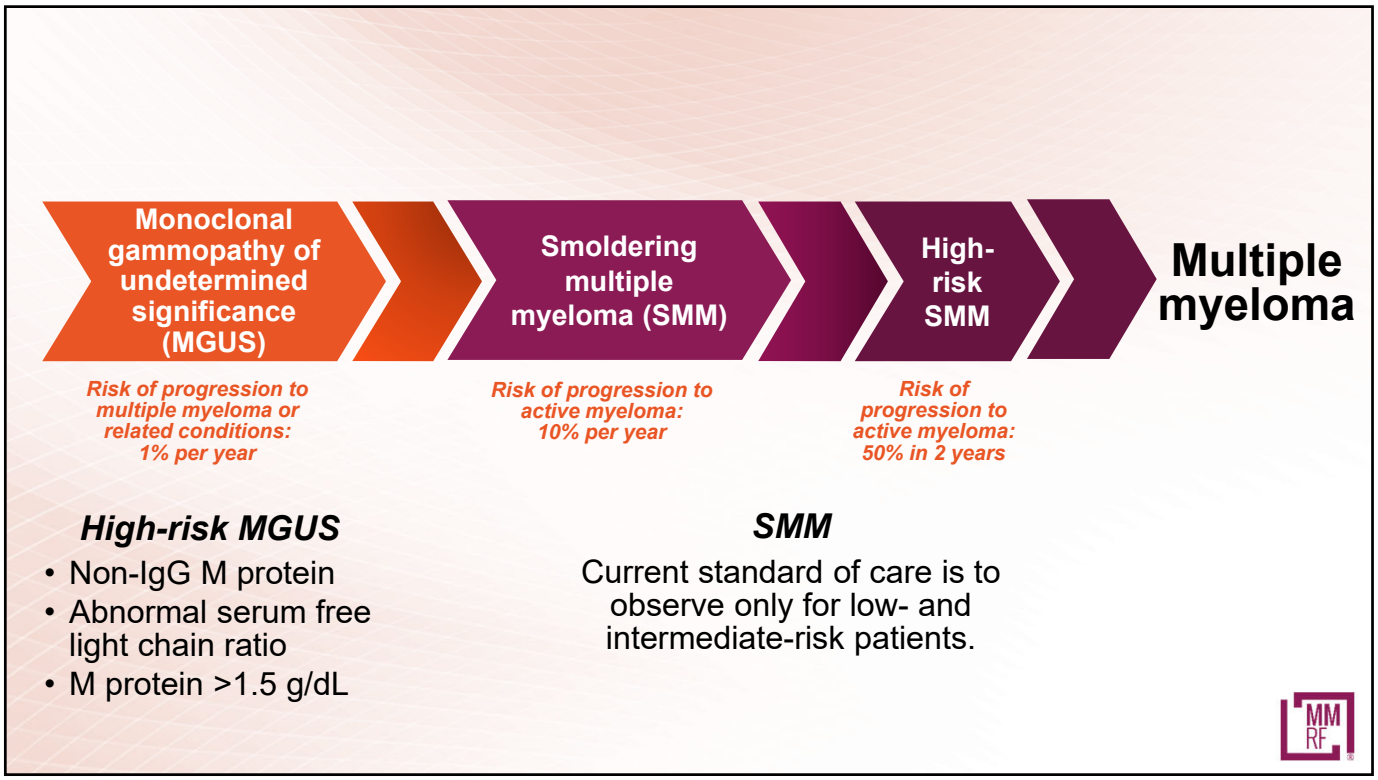

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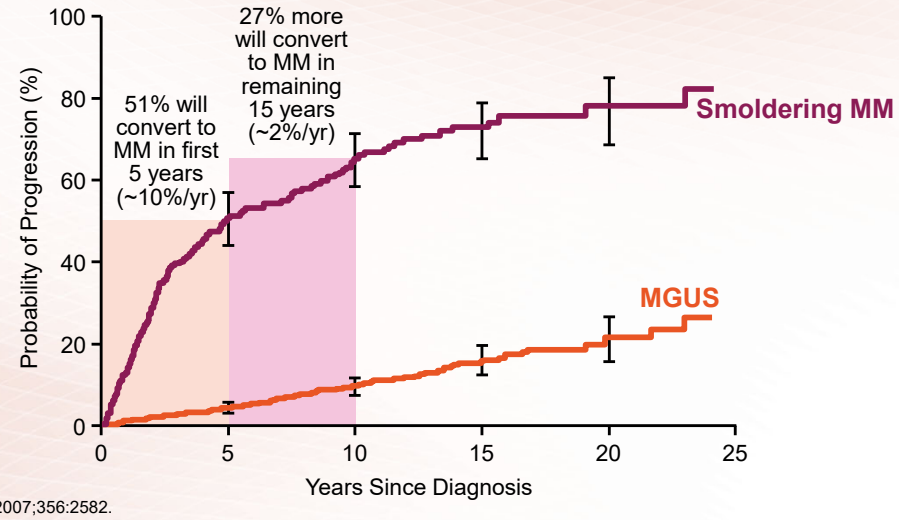
Smoldering Multiple Myeloma: Heterogeneous Disease



Kyle RA et al. *N Engl J Med*. 2007;356:2582.
Greipp PR et al. *J Clin Oncol*. 2005;23:3412.

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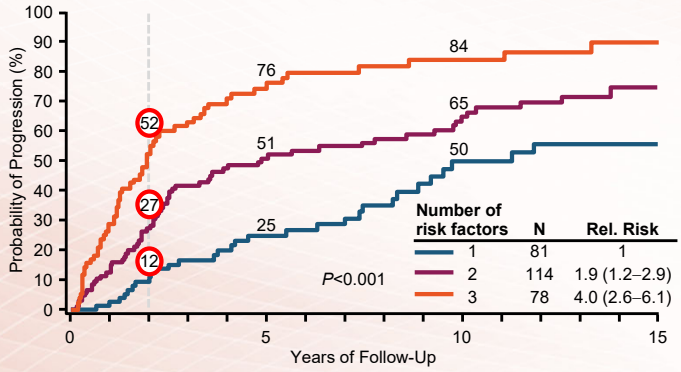
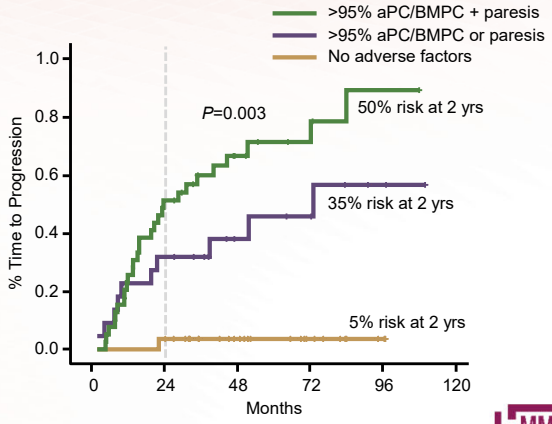
Risk Assessment in Smoldering Myeloma

Mayo risk model[1]
Plasma cell bone marrow infiltration, serum M-component level, and serum free light chain ratio



Spanish model[2]
Aberrant PCs by immunophenotype plus immunoparesis



1. Dispenzieri A et al. *Blood*. 2008;111:785.
2. Perez-Persona E et al. *Blood*. 2017;110:2586.

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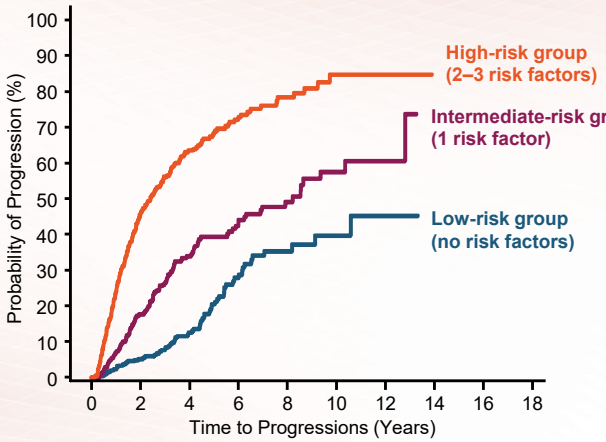
2/20/20 Model to Identify High-Risk SMM Patients

2/20/20 Risk assessment for SMM

- **2** >2 g/dL M protein
- **20** >20 free light chain ratio
- **20** >20% bone marrow plasma cells

Model does not include any biological or immune factors that may account for interpatient heterogeneity.



Risk of progression at 2 Years
44.2%
17.9%
6.2%

Mateos MV et al. *Blood Cancer J*. 2020;10:102.

62

Can we identify everyone who has a precursor condition?

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Identifying Patients With Myeloma Precursor Conditions

Nationwide Screening Studies

Iceland

iStopMM
Iceland Screens, Treats or Prevents Multiple Myeloma

United States and Canada

THE PROMISE STUDY

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Prevalence of MGUS and SMM

iStopMM Study

148,704 individuals 40 years of age or older in Iceland enrolled

75,422 screened for M protein and abnormal free light chain

3,725 individuals with MGUS

- **Arm 1** → **No further work-up**
- **Arm 2** → **Management by guidelines**
- **Arm 3: 1,279 patients** → **Intensive follow-up**

- 4.9% of individuals screened have MGUS
- 10.8% of individuals screened have SMM; SMM prevalence is 0.53%
- One third of SMM patients have an intermediate or high risk* of progression to myeloma

High prevalence of SMM has implications for future treatment policies and underlines the need for accurate risk stratification in SMM.

*Based on the 2/20/20 risk stratification model where three risk factors are associated with progression to active myeloma: (1) M protein levels, (2) free light chain ratio, and (3) the number of plasma cells in the bone marrow.

Thorsteinsdottir S et al. *Blood*. 2021;138. Abstract 151.

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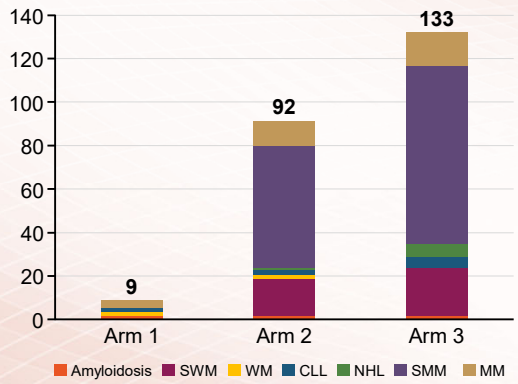
Additional iStopMM Study Findings



After 3 years of follow-up, active screening identifies a significantly higher number of individuals with malignancies and smoldering disease.

Kristinsson SY et al. *Blood*. 2021;138. Abstract 156.

MGUS was *not* associated with COVID-19 susceptibility or COVID-19 severity.

These findings suggest that immunosuppression in MGUS is different than in myeloma.

Rögnvaldsson S et al. *Blood*. 2021;138. Abstract 154.

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Promise Study Eligibility Criteria

2 groups of U.S. adults, age 30 or older, qualify for a free screening:

1. **African Americans**
   AND / OR
2. **People of Any Race Who Have a Parent, Sibling, or Child with:**
   Multiple myeloma, another blood cancer, OR one these related conditions:
   - Monoclonal Gammopathy of Undetermined Significance (MGUS)
   - Smoldering Multiple Myeloma
   - Waldenström Macroglobulinemia

We are also enrolling individuals who are 18 years of age or older and have a strong family history of blood cancer (2 or more first- and second-degree relatives).

Please sign up for the study if you qualify.

Note: The PROMISE study is for people who may have higher risks, **but have not been diagnosed** with any of these conditions.

If you have been diagnosed with one of these conditions, please visit our PCROWD study, a sister project for people with precursor conditions.

PCROWD

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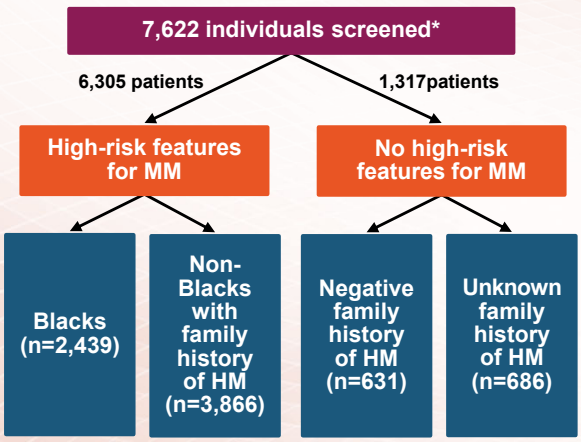
High Prevalence of Monoclonal Gammopathy in a Population at Risk

The PROMISE Study



- MGUS estimated in 13% to 17% of a high-risk screened population (rates increase with age).
- Higher detection rates of free light chains by mass spectrometry than conventional methods.
- Older adults who are Black or have a first-degree relative with a HM have an increased prevalence for MGUS.

Older individuals who are Black or have a first-degree relative with a HM may benefit from screening to allow for early detection and possible clinical intervention.

*The PROMISE study and Mass General Brigham Biobank—detected by mass spectrometry.
HM, hematologic malignancy
El-Khoury H et al. *Blood*. 2021;138. Abstract 152.

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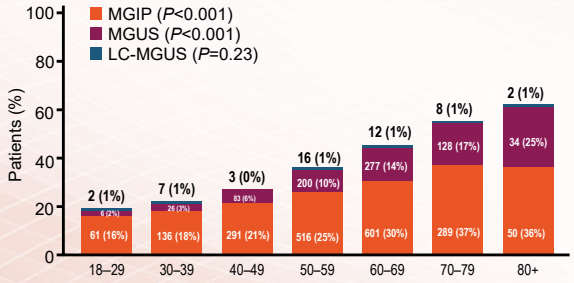
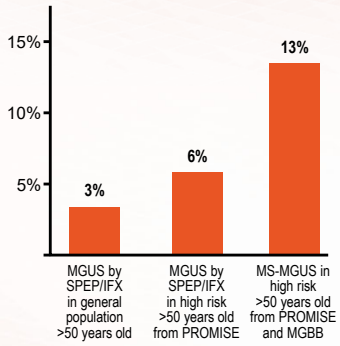
High Prevalence of Monoclonal Gammopathy in a Population at Risk

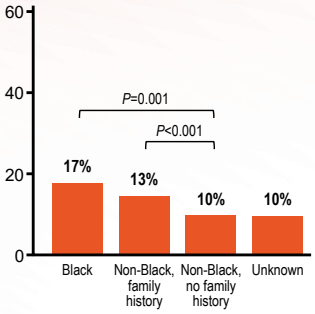
Rates of all monoclonal gammopathies* increase with age



MGUS more prevalent in individuals older than 50 years at risk



Higher rates of MGUS* in Blacks or individuals with a family history of HM and older than 50 years at risk



*Free light chains detected by mass spectrometry.

HM, hematologic malignancy; MGUS, monoclonal gammopathy of undetermined significance; MGIP, monoclonal gammopathies of indeterminate potential; LC, light chain; SPEP, serum protein electrophoresis; IFX, immunofixation; MS, mass spectrometry; MGBB, Mass General Brigham Biobank

El-Khoury H et al. *Blood*. 2021;138. Abstract 152.

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Therapeutic Intervention for SMM

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Overview of Treatment Approach

MGUS

Close monitoring (observation)

SMM

Close monitoring (observation)

If high risk: *possible* myeloma drugs?*

If bone loss: bone-targeting agents

Clinical trial participation should be considered

*Promising but only available as clinical trials.

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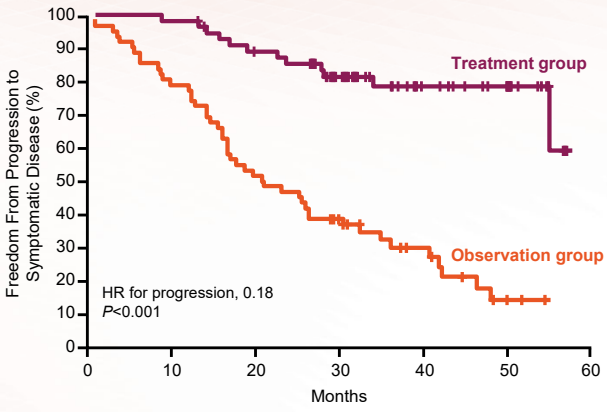
Early Therapeutic Intervention

Lenalidomide plus Dexamethasone for High-Risk Smoldering Multiple Myeloma

María-Victoria Mateos, M.D., Ph.D., Miguel-Teodoro Hernández, M.D., Pilar Giraldo, M.D., Javier de la Rubia, M.D., Felipe de Arriba, M.D., Ph.D., Lucía López Corral, M.D., Ph.D., Laura Rosiñol, M.D., Ph.D., Bruno Paiva, Ph.D., Luis Palomera, M.D., Ph.D., Joan Bargay, M.D., Albert Oriol, M.D., Felipe Prosper, M.D., Ph.D., Javier López, M.D., Ph.D., Eduardo Olavarría, M.D., Ph.D., Nuria Quintana, M.D., José-Luis García, M.D., Joan Bladé, M.D., Ph.D., Juan-José Lahuerta, M.D., Ph.D., and Jesús-F. San Miguel, M.D., Ph.D.

Progression-free survival for early treatment



HR, hazard ratio
Mateos MV et al. *N Engl J Med.* 2013;369:438.

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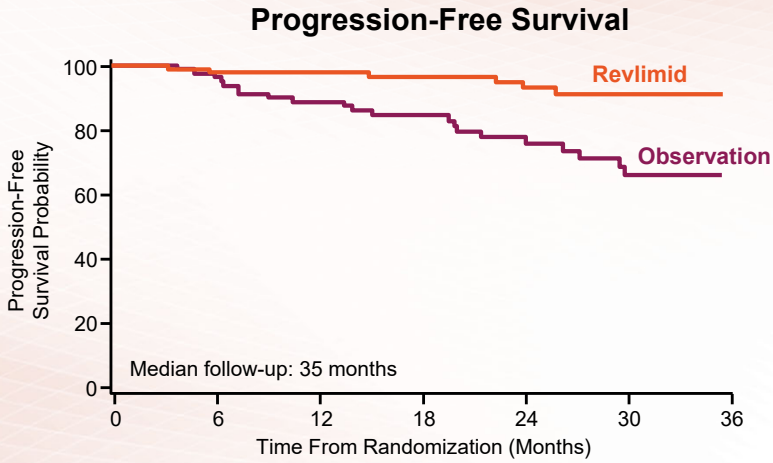
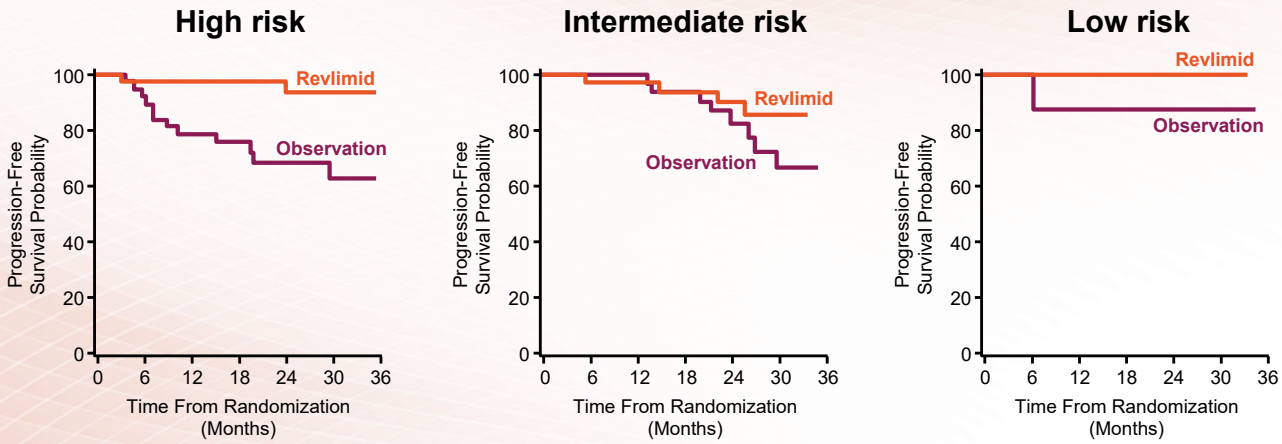
Revlimid vs Observation Alone in Patients With SMM



E3A06 Trial. Lonial S et al. *J Clin Oncol.* 2020;38:1126.

73

Phase 3 Progression-Free Survival by Mayo 2018 Risk Criteria



E3A06 Trial. Lonial S et al. *J Clin Oncol.* 2020;38:1126.

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Lessons Learned

- Early intervention improves PFS
- OS benefit seen in Spanish study
- Response rates of ~50% with lenalidomide alone leads to impressive PFS of >90% at 2 years
  - Does response matter as much in SMM?
- Many patients on observation also do quite well
  - How to identify them?
- Long-term therapy has toxicity implications and high rates of discontinuation

The Unknowns

- Would addition of a third (or fourth drug) in SMM lead to same benefit seen in NDMM?
  - Some high-risk patients with SMM are essentially MM patients
  - Deeper response should lead to better outcomes
- Is shorter but more intensified therapy better to limit long-term toxicity?
- What is the best intervention? Immunomodulatory drugs? Monoclonal antibodies? Proteasome inhibitors? Immunotherapy?

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Ongoing Clinical Studies for SMM Patients

Phases 1–3 or Observational

SMM patients at high risk of disease progression

- **Revlimid + dex ± Darzalex**
- Ninlaro + Revlimid + dex
- Darzalex (sc)
- Kyprolis + Revlimid + dex
- Empliciti + Revlimid + dex (E-PRISM Trial)
- Leflunomide
- Ninlaro + dex
- Pembrolizumab
- Kyprolis + Revlimid + Darzalex + dex (ASCENT trial)
- **Iberdomide ± dex**
- Darzalex + Revlimid + Velcade + dex (PRISM Trial)
- Sarclisa alone or + Revlimid
- Metformin
- Revlimid + dex ± Kyprolis
- Darzalex + Kyprolis + dex
- Vaccines: PVX-410, DKK1, custom-made
- Bispecifics
- Xgeva

SMM/MGUS

- PO Antibiotic trial (Emory)
- Predictors of progression (PROMISE study)
- Genomic and molecular predictors of progression (MD Anderson study)
- MMRF CureCloud
- Darzalex
- Metformin

Ask your doctor about whether you are a candidate for a clinical trial.

Trials found at www.clinicaltrials.gov

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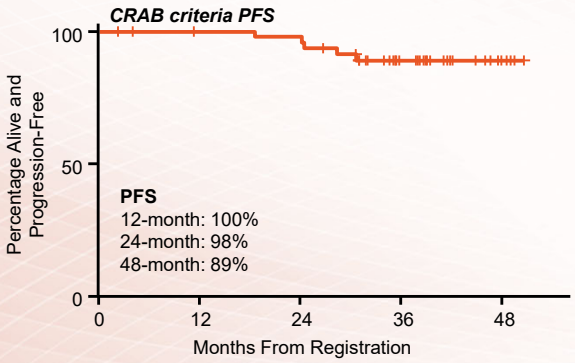
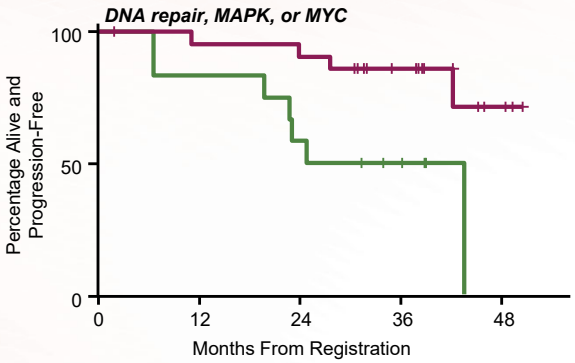
Precision Intervention With Empliciti in Smoldering Myeloma

Phase 2 Trial of Combination of Empliciti, Revlimid, and Dexamethasone in High-Risk Smoldering Multiple Myeloma (With Whole-Genome Sequencing of Patient Samples)

PFS in All Patients



PFS by High-Risk Mutations



E-PRISM Trial. Liu C-J et al. *Blood.* 2018;132. Abstract 154.

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GEM-CESAR: Multicenter, Open-Label, Phase 2 Trial of Kyprolis-Revlimid-dex

Response category	Induction (n=90)	HDT-ASCT (n=83)	Consolidation (n=81)	High risk (n=54)	Ultra-high risk (n=27)
ORR, n(%)	**85 (94%)**	**82 (99%)**	**81 (100%)**	**54 (100%)**	**27 (100%)**
≥CR	**37 (41%)**	**53 (64%)**	**61 (76%)**	**41 (76%)**	**20 (74%)**
VGPR	35 (39%)	18 (22%)	15 (19%)	10 (19%)	5 (19%)
PR	13 (14%)	11 (13%)	5 (6%)	2 (4%)	2 (7%)
SD	1 (1)	1 (1)	—	—	—
Progressive disease	2 (3%)	—	—	—	—
MRD negative	**27 (30%)**	**47 (56%)**	**51 (63%)**	**36 (67%)**	**15 (56%)**

Courtesy of MV Mateos.

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ASCENT: KRd-D

Primary end point: Rate of confirmed sCR
Secondary objectives: Safety, PFS, OS, MRD negativity

Study design

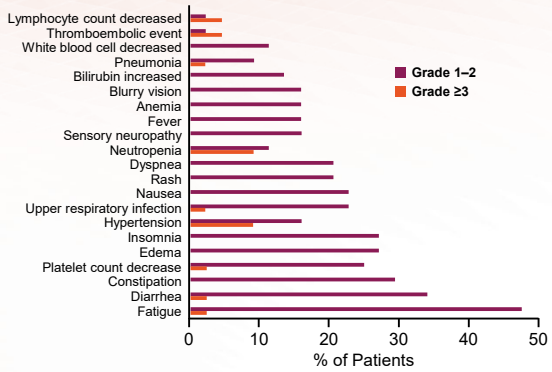
INDUCTION
(4-week cycles for 6 cycles)
- Carfilzomib (36 mg/m² twice weekly or 56 mg/m² weekly)
- Lenalidomide (25 mg daily for 3 weeks)
- Daratumumab (weekly for 8, every other week for 16 weeks)
- Dexamethasone 40 mg weekly

CONSOLIDATION
(4-week cycles for 6 cycles)
- Carfilzomib (36 mg/m² twice weekly or 56 mg/m² weekly)
- Lenalidomide (25 mg daily for 3 weeks)
- Daratumumab (every 4 weeks)
- Dexamethasone 20 mg weekly

MAINTENANCE
(4-week cycles for 12 cycles)
- Lenalidomide (10 mg daily for 3 weeks)
- Daratumumab (q 8 weeks)

Results to date:
- 54 patients accrued
- Median patient age 63 years
- 6% have completed maintenance, 56% consolidation, 80% induction, and 17% in induction phase
- ≥1 patient needed a dose modification
- ≥ grade 3 AE seen in 43% of patients

Toxicity profile



Quadruplet regimen KRd-D is well tolerated in high-risk SMM

AE, adverse event; CR, complete response; KRd-D, carfilzomib, lenalidomide, dexamethasone, daratumumab; MRD, minimal residual disease; sCR, stringent complete response

Kumar SK et al. *Blood*. 2020;136. Abstract 2285.

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Summary

- **Precursor plasma cell disorders are characterized by the presence of abnormal clonal plasma cells without any end organ damage.**
- **MGUS is a common condition; prevalence increases with age.**
- **There is variable risk of progression from MGUS and SMM to overt myeloma; several risk models can help predict who is at risk of progression. Screening efforts, particularly in high-risk populations, are under way.**
- **Growing data for benefit with early intervention.**
- **Patients with SMM should be offered treatment on clinical trials.**
- **Participation in observational/interventional studies is key to finding out which patients can benefit the most from early treatment and what is the best treatment to offer early.**

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Please take a moment to answer two questions about this presentation.

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Town Hall Questions & Answers

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MULTIPLE MYELOMA Research Foundation

Newly Diagnosed Multiple Myeloma

Amrita Y. Krishnan, MD
City of Hope Medical Center
Duarte, California

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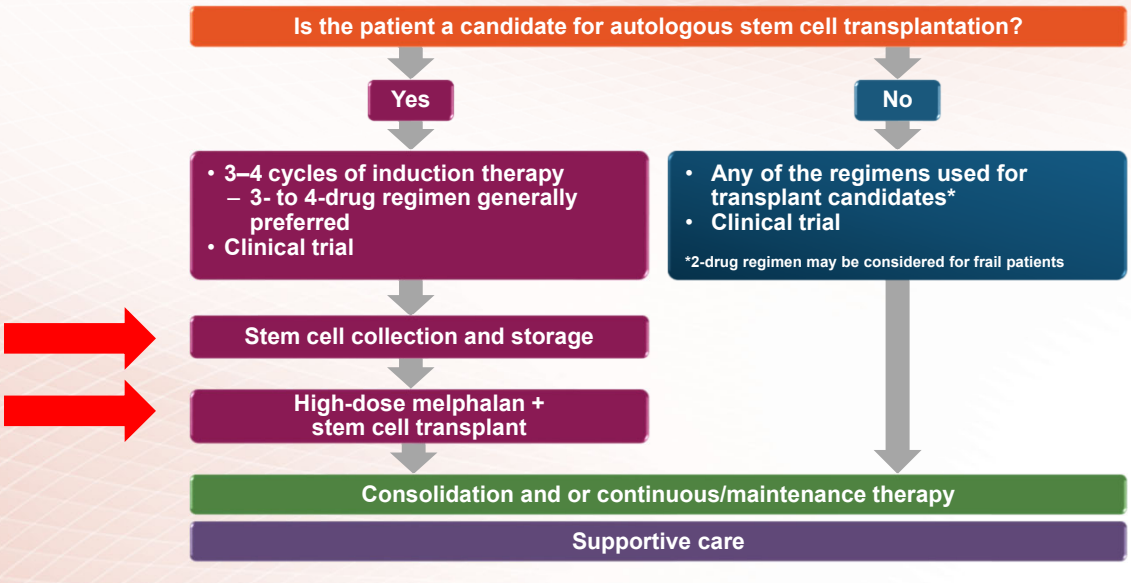
Overview of Treatment Approach for Active Multiple Myeloma



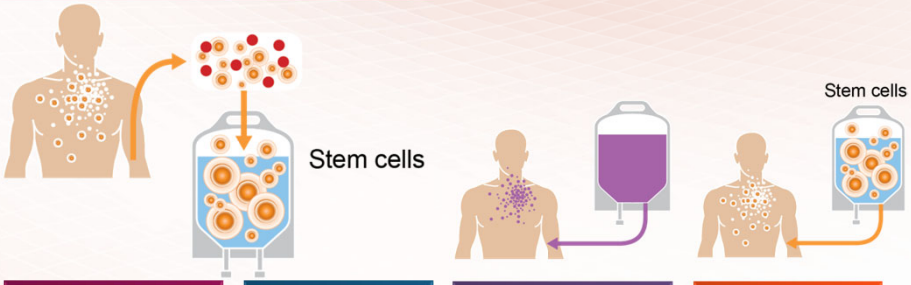
84

High-Dose Chemotherapy and Stem Cell Transplantation

- Offers durable remission based on current data
- Can be done as part of frontline therapy or at relapse (or both)
- More patients considered candidates than in the past, age is not a limiting factor

85

The Transplant Process



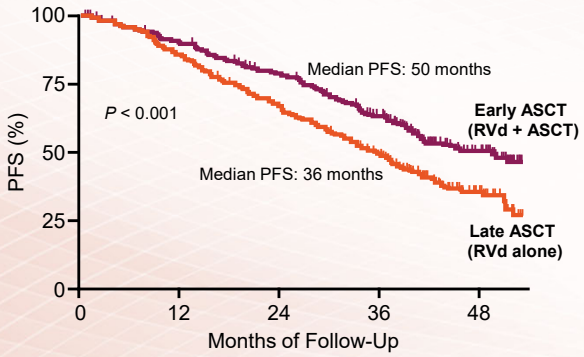
*The weeks leading up to the transplant; †The days after the transplant.

86

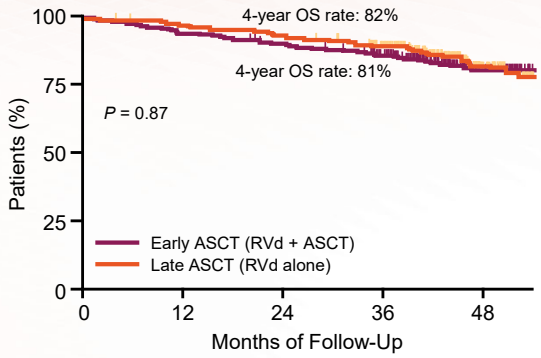
Should I get a transplant after induction therapy or should I wait until after I relapse? *Ongoing Clinical Trial*

Lenalidomide, Bortezomib, and Dexamethasone (RVd) With Transplantation for Myeloma (DETERMINATION Study): First Report

Progression-Free Survival (PFS)



Overall Survival (OS)



ASCT, autologous stem cell transplantation

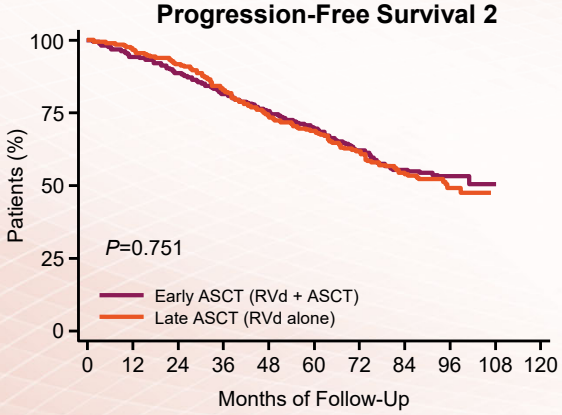
Attal M et al. *N Engl J Med*. 2017;376:1311.
Perrot A et al. *Blood* 2020;136. Abstract 143.

87

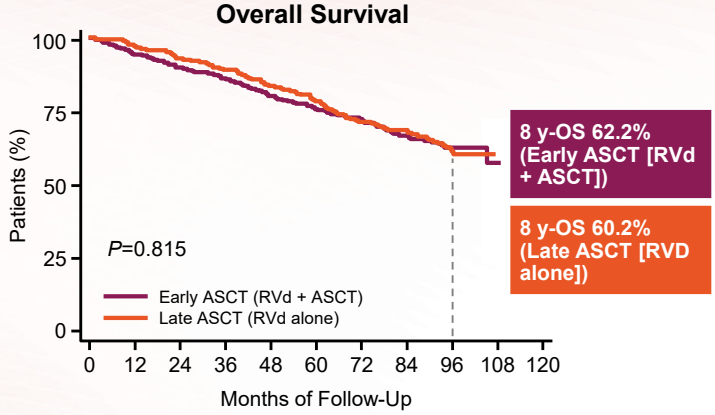
Should I get a transplant after induction therapy or should I wait until after I relapse? *Ongoing Clinical Trial*

Lenalidomide, Bortezomib, and Dexamethasone (RVd) With Transplantation for Myeloma (DETERMINATION Study): Updated (Long-Term) Report

Progression-Free Survival 2



Overall Survival



Attal M et al. *N Engl J Med*. 2017;376:1311.
Perrot A et al. *Blood* 2020;136. Abstract 143.

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Early vs Delayed Transplant Pros and Cons

Pros

Early ASCT

- Youngest you are going to be
- Healthiest you are going to be
- Allows for fewer cycles of initial treatment
- Deeper and more durable response

Delayed ASCT

- Conserve quality of life in the early part of disease journey
- Minimize disruption to lifestyle
- If there is residual disease after completed combination therapy, PFS may be shorter with delayed (vs early) hematopoietic cell transplantation (HCT), but OS is the same

Cons

Early ASCT

- 20% of patients still relapse within 2 years
- 1% risk of serious life-threatening complications
- 3 months of full clinical recovery
- No proven impact on overall survival

Delayed ASCT

- 60%–70% of patients will relapse and may need it as salvage
- Not all patients relapsing are unable to undergo salvage HCT
- May need longer duration of chemotherapy to replace its effects

89

Autologous Stem Cell Transplantation
Summary

Autologous stem cell transplantation (ASCT) remains the standard of care for frontline myeloma therapy for patients who are eligible; its safety has been established and it induces long remissions.

90

What is maintenance therapy?

- A prolonged, and often low-dose, treatment given to myeloma patients after achieving a desired response to initial therapy
- To prevent disease progression for as long as possible while maintaining favorable quality of life
- To deepen responses by reducing minimal residual disease (MRD) or maintaining the response achieved, reduce the risk of relapse, and prolong survival

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Successful Maintenance Therapy Must...

1. Be convenient
2. Be safe and well tolerated long term
3. Not interfere with the use of other future treatments

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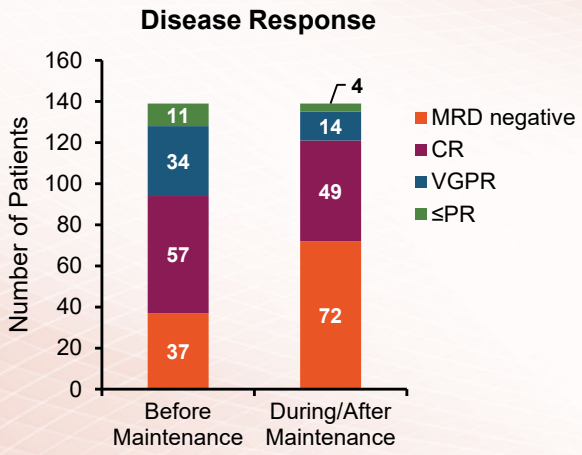
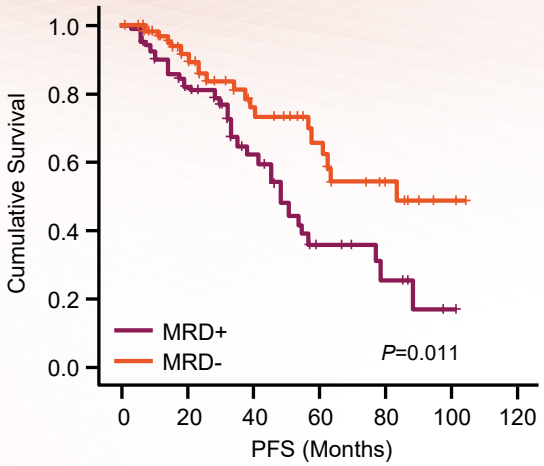
Revlimid Maintenance Therapy: Improves Depth of Response





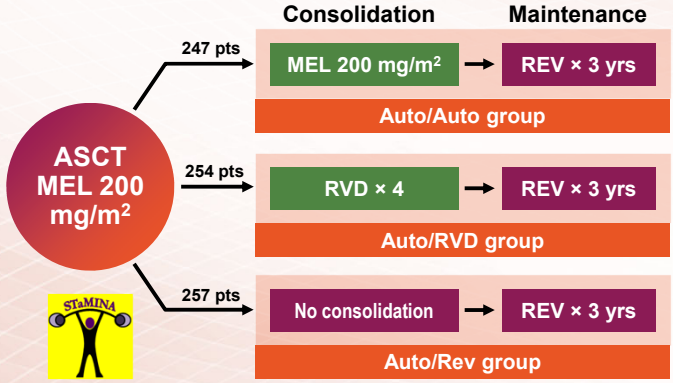
At maximal response during or after maintenance treatment with Revlimid

Alonso R et al. *Blood Adv*. 2020;4:2163.

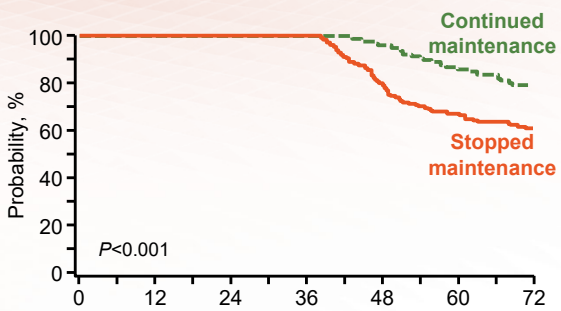
93

Revlimid Maintenance Duration

STAMINA Trial (BMT-CTN0702)



There was no difference in PFS or OS between the 3 groups



Discontinuation of Revlimid @ 3 years did not impact overall second primary malignancies (SPM) rates @ 6 years

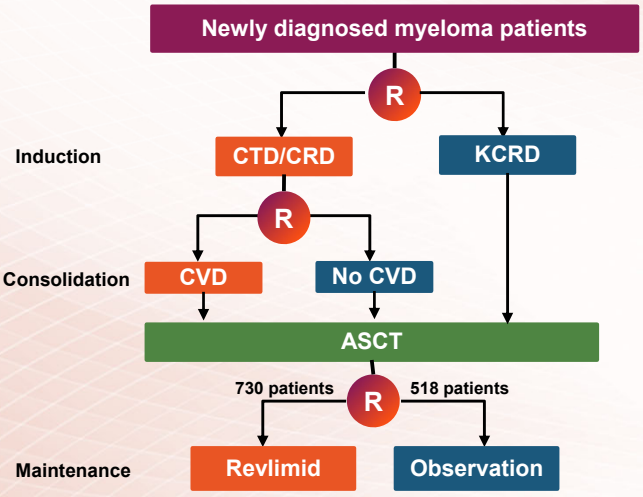
Discontinuation of Revlimid maintenance at 3 years is not recommended because of the increased risk of disease progression

MEL, melphalan; RVD, Revlimid-Velcade-dex; REV, Revlimid
STAMINA Trial. Stadtmauer EA et al. *J Clin Oncol*. 2019;37:589; Hari P et al. *J Clin Oncol*. 2020;38. Abstract 8506.

94

Maintenance Duration

Myeloma XI Study



Median PFS (mos)	At time of randomization to maintenance therapy (median follow up 44.7 mos)
	All patients*
Revlimid	64
Observation	32
Hazard ratio	0.52
P Value	<0.001

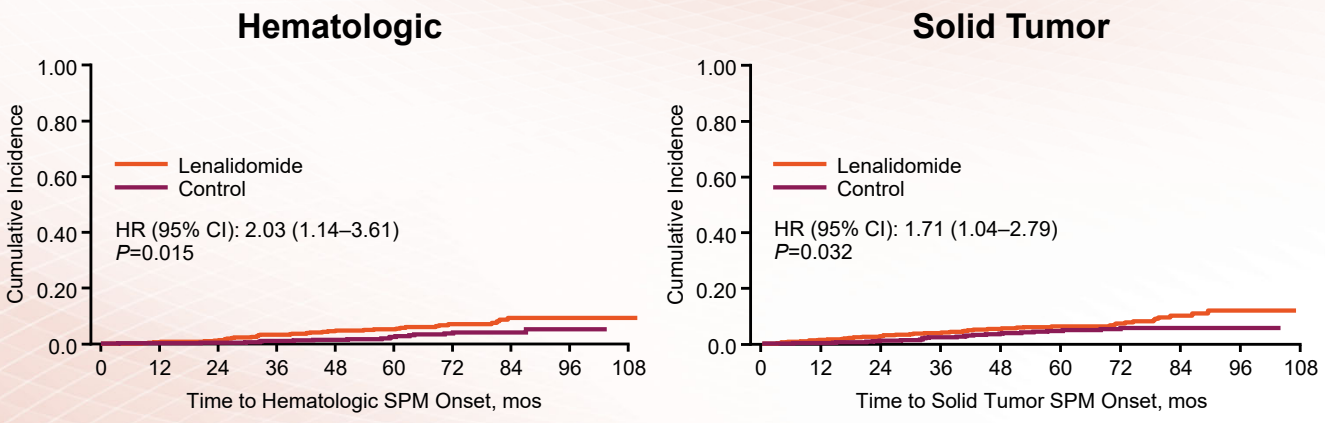
*PFS benefit across all patient subgroups on Revlimid maintenance therapy: standard risk; molecular high risk which included the presence of del(17p), gain(1q), t(4;14), t(14;16), or t(14;20); MRD positive; and MRD negative.

More evidence for the benefit of longer duration of Revlimid maintenance in patients who are MRD positive than MRD negative. And evidence of ongoing benefit beyond 2–3 years for patients with both standard- and high-risk disease.

Myeloma XI Study. Pawlyn C et al. *Blood*. 2022;140. Abstract 570.

95

Revlimid Maintenance: Cumulative Incidence of Second Primary Malignancies



McCarthy PL et al. *J Clin Oncol*. 2017;35:3279.

96

Continuous or Maintenance Therapy Options

	Preferred	Recommended	Certain circumstances
Transplant eligible	• Revlimid*	• Velcade • Darzalex • Ninlaro	• Velcade-Revlimid ± dex • Kyprolis-Revlimid
Transplant ineligible	• Revlimid*	• Velcade • Ninlaro	• Velcade-Revlimid

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
National Comprehensive Cancer Network Guidelines Version 2.2023. Multiple Myeloma.

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Maintenance Therapy
Summary

- **The body of evidence from phase 3 trials indicates that maintenance therapy improves PFS and likely OS and should be given until progression.**
- **Most patients should receive maintenance with some agent if able to tolerate the side effects.**
- **Minimizing side effects and maximizing quality of life are essential to the success of maintenance therapy.**
- **For patients who are unable to tolerate Revlimid, there are other agents such as Pomalyst, Ninlaro, Kyprolis, Velcade, and Darzalex that are effective, but they are not yet FDA-approved for use as maintenance. Several clinical trials are under way.**

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Minimal Residual Disease Negativity as a Multiple Myeloma Treatment Goal

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Goals of Multiple Myeloma Therapy

- Reduce the amount of M protein (as measured by serum protein electrophoresis) or light chains (as measured via the free light chain test) to the lowest level possible
- **Eliminate myeloma cells from the bone marrow (as measured via minimal residual disease [MRD] testing)**
- Improve quality of life with as few treatment side effects as possible
- Provide the longest possible period of response before first relapse
- Prolong overall survival

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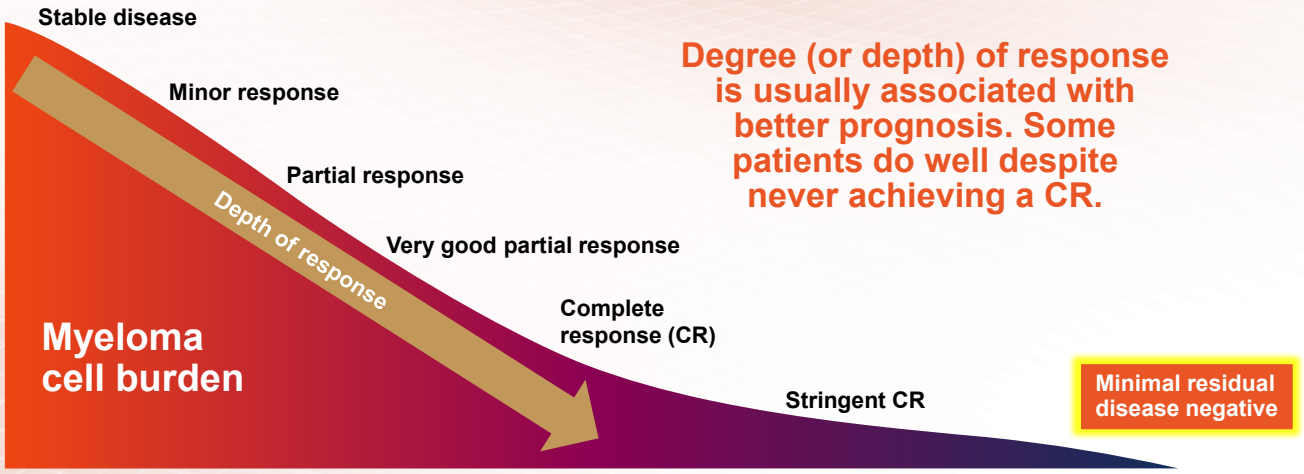
Measuring Response to Therapy



Degree (or depth) of response is usually associated with better prognosis. Some patients do well despite never achieving a CR.

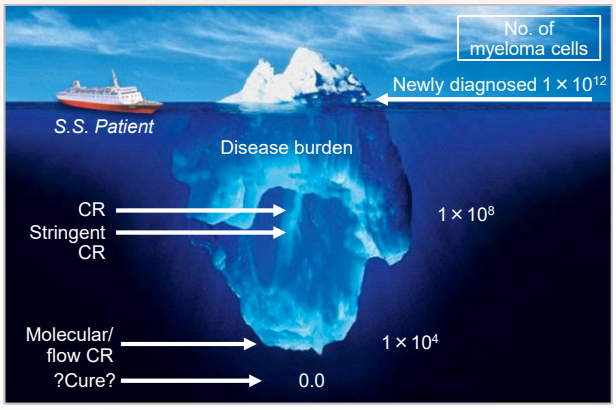
ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients

Palumbo A et al. *J Clin Oncol*. 2014;32:587.
Kumar S et al. *Lancet Oncol*. 2016;17:e328.

101

Why do we need to MRD?

- With new and more effective treatments, more patients achieve CR
- However, achieving a CR does not necessarily mean that all myeloma cells are gone
- Routine blood tests are not sensitive enough to detect these remaining cells



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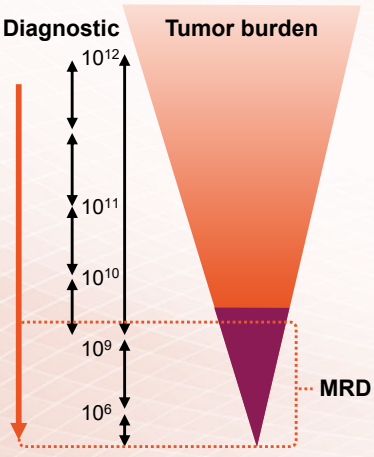
What is MRD?

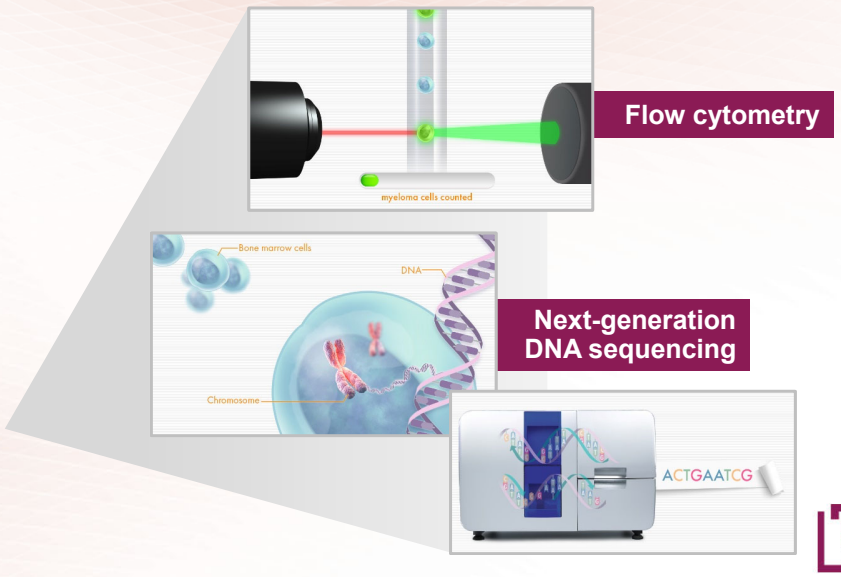
The presence of small amounts of myeloma cells left in the bone marrow following the achievement of a CR after treatment

MRD tests can detect at least 1 cell in 100,000 or better. Ideally, we want to use more sensitive assays that can find 1 cell in a million

103

How is MRD measured?





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Key Terms for MRD

MRD positive or MRD positivity (MRD+)	MRD negative or MRD negativity (MRD-)
• Myeloma cells are still detected	• Myeloma cells are not detected

Level of sensitivity can be different depending on methodology used: next-generation sequencing (NGS) or next-generation flow cytometry (NGF).

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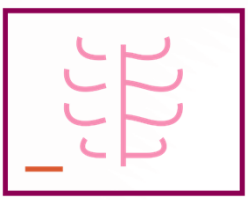
Comprehensive Response Assessment

Right now, measurement of MRD depends on counting cells in bone marrow samples

What about other areas of the body?

Imaging (with PET/CT scan) is also required to detect residual disease outside of the bone marrow



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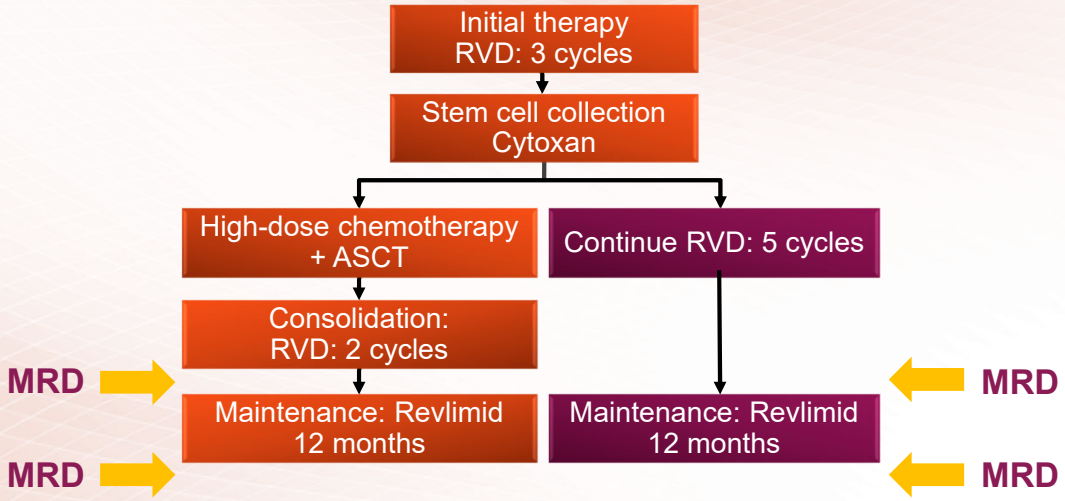
Why is it important to achieve MRD negativity?

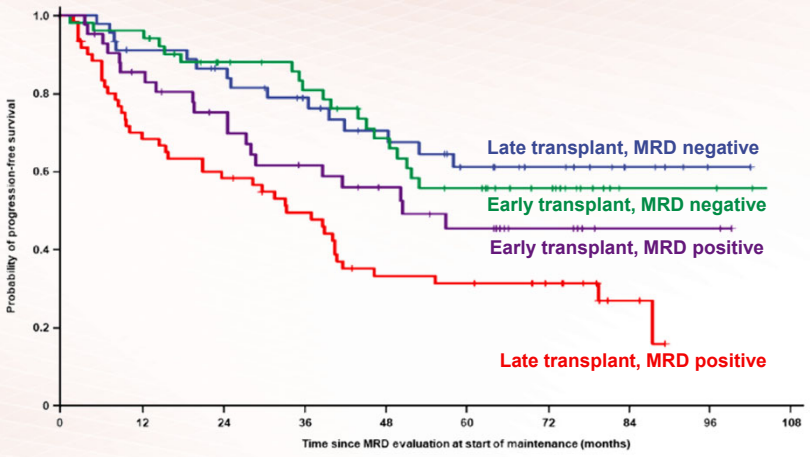


RVD, Revlimid, Velcade, dexamethasone; Cytoxan, cyclophosphamide
MRD by next-generation sequencing (sensitivity 1 × 10^{-5})
Determination Study. Richardson PG et al. *N Engl J Med*. 2022;387:132.

107

Why is it important to achieve MRD negativity?

Patients who achieve MRD negativity following treatment experience longer remission than those who are still MRD positive after treatment.



MRD by next-generation sequencing (sensitivity 1 × 10^{-5})
Determination Study. Richardson PG et al. *N Engl J Med*. 2022;387:132.

108

Patients Who Achieve MRD Negativity Following Treatment Live Longer Than Those Who Are MRD Positive

Key points from 14 studies analyzed*

- Being MRD negative is correlated with longer progression-free and overall survival.
- MRD negativity may not (?) carry the same weight in patients with standard-risk vs high-risk disease.

*5 trials included stem cell transplantation/10 studies included maintenance

Munshi NC et al. *JAMA Oncol*. 2017;3:28.

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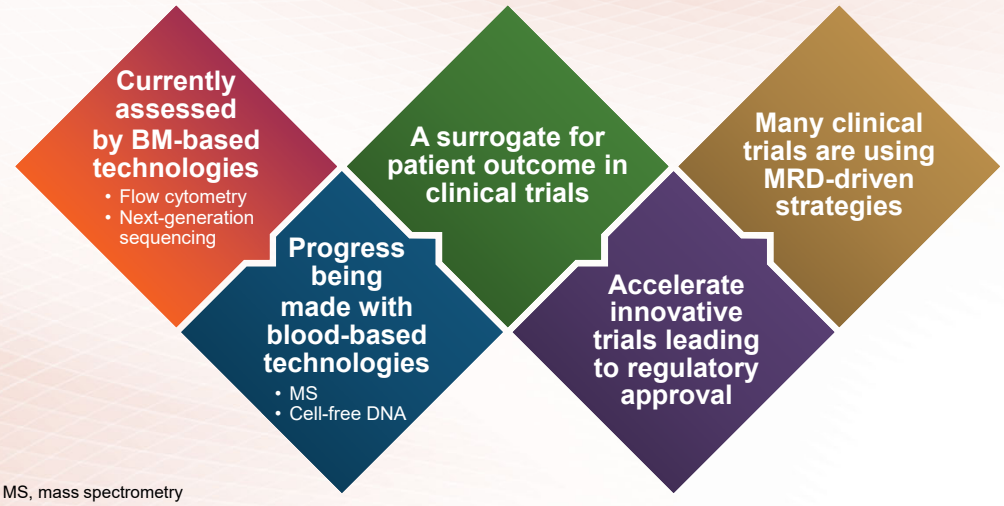
MRD Is Important for Clinical Care and New Drug Registration

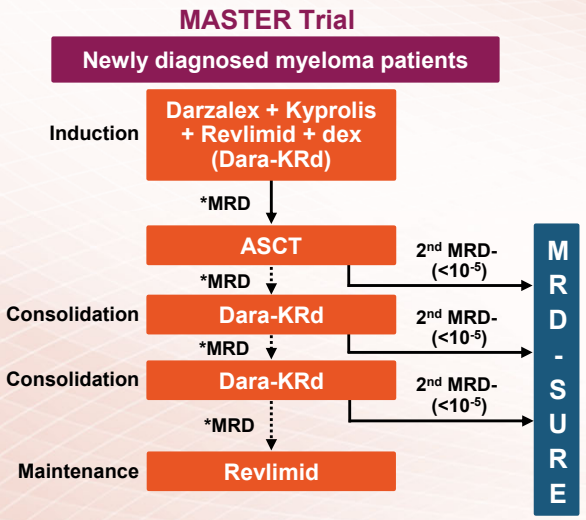


BM, bone marrow; MS, mass spectrometry

Anderson KC et al. *Clin Cancer Res*. 2021;27:5195.
Costa LJ et al. *Leukemia*. 2021;35:18.

110

MRD Response-Adapted Consolidation and Treatment Cessation



- 80% of patients achieved MRD negativity (at <1 × 10^{-5}) and 66% achieved MRD negativity at <1 × 10^{-6}.
- 86% of patients achieved a CR or better.
- Responses deepened with each phase of treatment—and were similar in patients with zero, one, or two or more high-risk genetic abnormalities.
- ASCT increased the rates of MRD negativity following induction therapy, benefitting patients with highest-risk disease features.

Nearly all patients with no or only one high-risk genetic abnormality and confirmed MRD negativity had no disease progression or MRD resurgence since stopping treatment.

*24 and 72 weeks after completion of therapy (by next-generation sequencing)

Costa LJ et al. *Blood*. 2021;138. Abstract 481; Costa LJ et al. *J Clin Oncol*. 2021; Dec 13 [epub ahead of print].

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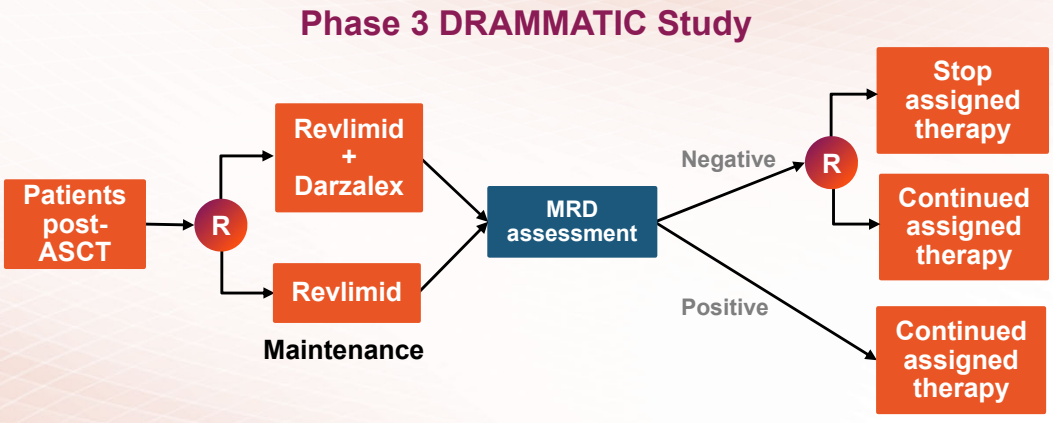
Ongoing Study Using MRD Results to Direct Therapy



Primary end point: overall survival
Secondary end points: frequency and rate of toxicity; progression-free survival; best overall response; rate of MRD negativity; quality of life

https://clinicaltrials.gov/ct2/show/NCT04071457.

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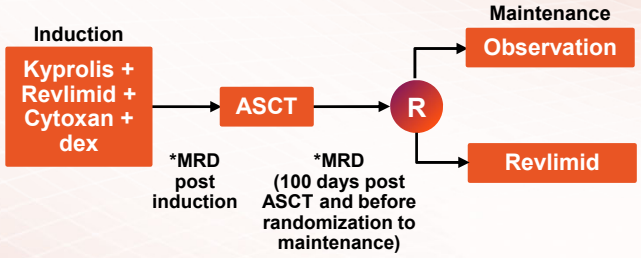
Potential Blood-Based MRD Testing: Mass Spectrometry



MRD is currently measured using a bone marrow sample; myeloma cells are detected using one of two methodologies: (1) flow cytometry or (2) next-generation sequencing.

Mass spectrometry (MS) is being evaluated as a method to detect free light chains (FLCs) in the blood as a potentially more sensitive test to detect MRD in patients after therapy.

MS positivity was associated with patients having a shorter time until disease progression compared to being MS negative.

In patients who achieved a CR or sCR, 16% to 34% were MS positive following induction, ASCT, or prior to maintenance; these patients also had a shorter time until disease progression compared to being MS negative and in CR/sCR.

Some patients who were MRD negative* and also MS positive also had a shorter time until disease progression compared to being MRD negative and MS negative.

MS may provide a useful alternative to bone marrow testing to detect MRD in patients and may even help to identify patients at increased risk of early relapse if they are MRD negative but MS positive during maintenance therapy.

*By flow cytometry at a sensitivity of 4×10^{-5}

Giles HV et al. *Blood*. 2021;138. Abstract 820.

113

Minimal Residual Disease
Summary

- **MRD is the deepest response after myeloma treatment, including bone marrow MRD and imaging MRD. NGF and NGS are the two most commonly used marrow MRD tests. Blood-based MRD is in exploration.**
- **MRD has been associated with longer progression-free and overall survival to predict lower risk of progression. Modern combination therapies show increasingly higher MRD negativity rate.**
- **MRD response–directed therapy has been applied in more and more clinical trials to explore how to guide treatment decisions in myeloma.**
- **MRD is also useful as an end point in clinical trials helping to expedite new drug approval in myeloma.**

MRD, minimal residual disease; NGF, next-generation flow cytometry; NGS, next-generation sequencing

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MULTIPLE MYELOMA Research Foundation

Relapsed/Refractory Multiple Myeloma and Treatments on the Horizon

Paul G. Richardson
Dana-Farber Cancer Institute
Boston, Massachusetts

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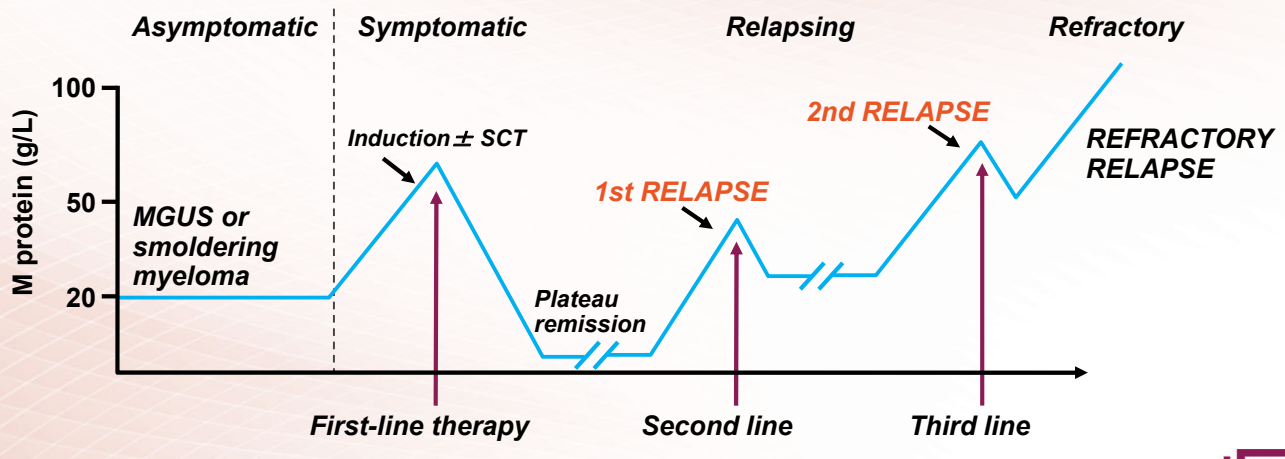
Multiple Myeloma Is a Marathon, Not a Sprint



Adapted from Borrello I. *Leuk Res*. 2012;36 Suppl. 1:S3.

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Definitions: What is relapsed/refractory disease and a line of therapy?

- ***Relapsed:*** recurrence (reappearance of disease) after a response to therapy
- ***Refractory:*** progression despite ongoing therapy
- ***Progression:*** change in M protein/light chain values
- ***Line of therapy:*** change in treatment due to either progression of disease or unmanageable side effects
  - **Note:** initial (or induction) therapy + stem cell transplant + consolidation/ maintenance therapy = 1 line of therapy

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Biochemical Relapse or Clinical Relapse

Biochemical

- Patients with asymptomatic rise in blood or urine M protein, free light chains, or plasma cells

→ **Timing of therapy initiation/escalation dependent on many factors**

Clinical

- Based on direct indicators of increasing disease and/or end-organ dysfunction

→ **Requires immediate initiation/escalation of therapy**

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Choosing Therapy for First or Second Relapse

Choices are broadest and guided by

- Disease biology
- Nature of relapse
- Patient preference

Factors to consider

- Prior autologous stem cell transplant
- Prior therapies
- Aggressiveness of relapse
- Comorbidities
- Psychosocial issues
- Access to care

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Options for Relapsed/Refractory Disease Continue to Increase

IMiDs	Proteasome inhibitors	Chemotherapy anthracyclines	Chemotherapy alkylators	Steroids	Novel mechanisms of action	Monoclonal antibodies	Cellular therapy
Thalomid (thalidomide)	Velcade (bortezomib)	Adriamycin	Cytoxan (cyclophosphamide)	Dexamethasone	XPOVIO (selinexor)	Empliciti (elotuzumab)	Abecma (idecabtagene vicleucel)
Revlimid (lenalidomide)	Kyprolis (carfilzomib)	Doxil (liposomal doxorubicin)	Bendamustine	Prednisone	Venclexta (venetoclax)*	Darzalex (daratumumab)	Carvykti (ciltacabtagene autoleucel)
Pomalyst (pomalidomide)	Ninlaro (ixazomib)		Melphalan		~~Farydak (Panobinostat)~~†	Sarclisa (isatuximab)	
					~~Pepaxto (melflufen)~~†	~~Blenrep (belantamab mafodotin)~~†‡	
						Tecvayli (teclistamab)§	

*Not yet FDA-approved for patients with multiple myeloma; †Withdrawn from the US market; ‡Antibody-drug conjugate; §Bispecific antibody

New formulations, new dosing, and new combinations, too!

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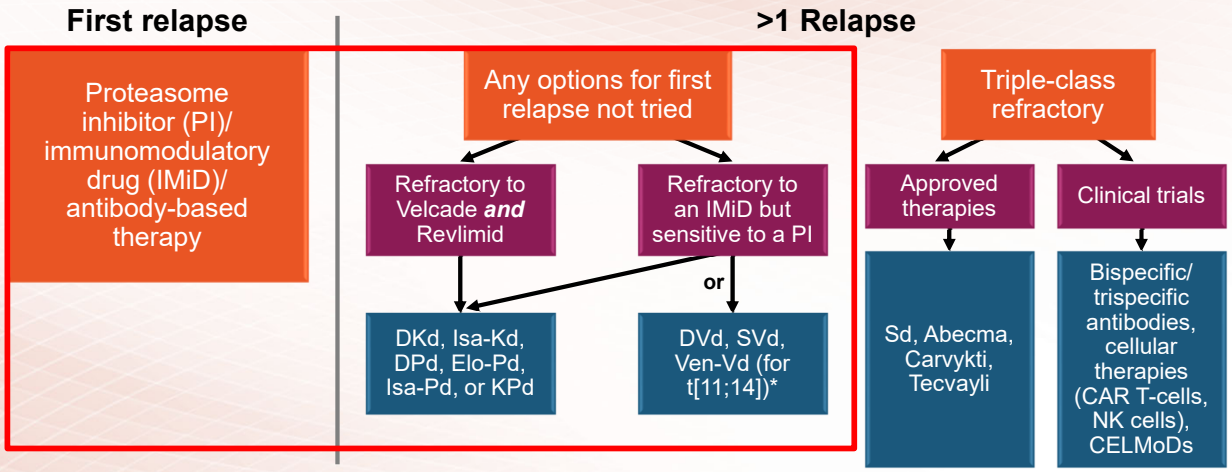
Treatment Approach



D, daratumumab (Darzalex); K, carfilzomib (Kyprolis); d, dexamethasone; Isa, isatuximab (Sarclisa); P, pomalidomide (Pomalyst); Elo, elotuzumab (Empliciti); V, bortezomib (Velcade); S, selinexor (Xpovio); Ven, venetoclax (Venclexta)

*Not yet approved for use in myeloma patients.

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Proteasome Inhibitor– and Immunomodulatory Drug–Based Regimens for Early Relapse

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Currently Available Agents for One to Three Prior Lines of Therapy

Drug	Formulation		Approval
Velcade (bortezomib)		• IV infusion • SC injection	• For **relapsed/refractory** myeloma
Kyprolis (carfilzomib)		• IV infusion • Weekly dosing	• For **relapsed/refractory** myeloma as a single agent, as a doublet with dexamethasone, and as a triplet with Revlimid or Darzalex plus dexamethasone
Ninlaro (ixazomib)		Once-weekly pill	• For **relapsed/refractory** myeloma as a triplet with Revlimid and dexamethasone
Revlimid (lenalidomide)*		Once-daily pill	• For **relapsed/refractory** myeloma in combination with dexamethasone
Pomalyst (pomalidomide)*		Once-daily pill	• For **relapsed/refractory** myeloma in combination with dexamethasone
XPOVIO (selinexor)		Once-weekly pill	• For **relapsed/refractory** myeloma as a triplet with Velcade and dexamethasone

*Black box warnings: embryo-fetal toxicity; hematologic toxicity (Revlimid); venous and arterial thromboembolism

IV, intravenous; SC, subcutaneous

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Proteasome Inhibitor– and Immunomodulatory Drug–Based Regimens for Early Relapse

	OPTIMISMM	ASPIRE	TOURMALINE-MM1	BOSTON
Regimens compared	• Velcade-Pomalyst-dex (VPd) vs Vd	• Kyprolis-Revlimid-dex (KRd) vs Rd	• Ninlaro-Rd (IRd) vs Rd	• XPOVIO-Velcade-dex (XPO-Vd) vs Vd
Median progression-free survival favored	• VPd: 11 vs 7 months	• KRd: 26 vs 17 months	• IRd: 21 vs 15 months	• XPO-Vd: 14 vs 9 months
Clinical considerations	• Consider for relapse on Revlimid • VPd associated with more low blood counts, infections, and neuropathy than Pd	• KRd associated with more upper respiratory infections and high blood pressure than Rd	• IRd an oral regimen • Gastrointestinal toxicities and rashes • Lower incidence of peripheral neuropathy	• XPO-Vd associated with low platelet counts and fatigue with triplet, but less neuropathy than the Vd

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Important Considerations for Use of Proteasome Inhibitors and Immunomodulatory Drugs

Proteasome Inhibitors

Velcade

- Risk of **peripheral neuropathy (PN;** numbness, tingling, burning sensations and/or pain due to nerve damage)
  - Avoid in patients with severe existing PN
  - Reduced with subcutaneous once-weekly dosing
- High risk of **shingles**
  - Use appropriate vaccination
- No dose adjustment for kidney issues; adjust for liver issues

Kyprolis

- Less **PN** than Velcade
- High risk of **shingles**
  - Use appropriate vaccination
- Monitor for **heart, lung, and kidney side effects**
  - Use with caution in older patients with cardiovascular risk factors
- High blood pressure
- No dose adjustment for kidney issues; adjust for liver issues

Ninlaro

- Less **PN** than Velcade
- High risk of **shingles**
  - Use appropriate vaccination
- Monitor for rashes and **gastrointestinal (GI)** side effects
  - GI effects occur early
- Needs to be taken at least 1 hour before or 2 hours after a meal

Immunomodulatory Drugs

Revlimid*

- **Rash**
  - Consider antihistamines
- **Diarrhea**
  - Consider bile acid sequestrants
- Risk of **blood clots**
- Risk of second primary **malignancies**
- Dose adjustment based on kidney function

Pomalyst*

- **Low blood counts**
- Less **rash** than Revlimid
- Risk of second primary **malignancies**
- Risk of **blood clots**

*Black box warning

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Important Considerations for Use of XPOVIO

Gastrointestinal

Begin prophylactic anti-nausea medications.
Consult with your doctor if nausea, vomiting, or diarrhea occur or persist.

Low sodium (hyponatremia)

Maintain fluid intake.
Salt tabs

Fatigue

Stay hydrated and active.

Low blood counts (cytopenias)

Report signs of bleeding right away.
Report signs of fatigue or shortness of breath.

Chari A et al. *Clin Lymphoma Myeloma Leuk*. 2021;21:e975.

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Monoclonal Antibody–Based Regimens at Relapse

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Currently Available Naked Monoclonal Antibodies for One to Three Prior Lines of Therapy

Drug	Formulation		Approval
Darzalex (daratumumab)		SC once a week for first 8 weeks, then every 2 weeks for 4 months, then monthly	• For **relapsed/refractory** myeloma as a single agent and as a triplet with Revlimid or Velcade or Kyprolis or Pomalyst plus dexamethasone
Empliciti (elotuzumab)		IV once a week for first 8 weeks, then every 2 weeks (or every 4 weeks with pom)	• For **relapsed/refractory** myeloma as a triplet with Revlimid or Pomalyst and dexamethasone
Sarclisa (isatuximab)		IV once a week for first 4 weeks, then every 2 weeks	• For **relapsed/refractory** myeloma as a triplet with Pomalyst or Kyprolis and dexamethasone

IV, intravenous; SC, subcutaneous

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Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

	POLLUX	CASTOR	CANDOR	APOLLO
Regimens compared	• Darzalex-Revlimid-dex (DRd) vs Rd	• Darzalex-Velcade-dex (DVd) vs Vd	• Darzalex-Kyprolis-dex (DKd) vs Kd	• Darzalex-Pomalyst-dex (DPd) vs Pd
Median progression-free survival favored	• DRd: 45 vs 18 months	• DVd: 17 vs 7 months	• DKd: 29 vs 15 months	• DPd: 12 vs 7 months
Clinical consider-ations	• Consider for relapses from Revlimid or Velcade maintenance • DRd associated with more upper respiratory infections, low blood white blood cell counts, and diarrhea	• Consider for patients who are Revlimid-refractory without significant neuropathy • DVd associated with more low blood cell counts	• Consider for younger, fit patients who are double-refractory to Revlimid and Velcade • DKd associated with more respiratory infections • Sever side effects (possibly fatal) in intermediate fit patients 65 and older	• Consider in patients who are double-refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro) • Severe low white blood cell counts

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Monoclonal Antibody–Based Regimens for Early Relapse: Sarclisa and Empliciti

	ELOQUENT-2	ELOQUENT-3	ICARIA-MM	IKEMA
Regimens compared	• Empliciti-Revlimid-dex vs Rd	• Empliciti-Pomalyst-dex vs Pd	• Sarclisa-Pomalyst-dex vs Pd	• Sarclisa-Kyprolis-dex vs Kd
Median progression-free survival favored	• Empliciti-Rd: 19 vs 15 months	• Empliciti-Pd: 10 vs 5 mos	• Sarclisa-Pd: 12 vs 7 mos	• Sarclisa-Kd: 42 vs 21 mos
Clinical consider-ations	• Consider for non-Revlimid refractory, frailer patients • Overall survival benefit with Empliciti-Rd • Empliciti-Rd associated with more infections	• Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)	• Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro) • Sarclisa-Pd associated with severe low white blood cell counts, more dose reductions, upper respiratory infections, and diarrhea	• Consider for patients refractory to Revlimid and Velcade • Sarclisa-Kd associated with higher MRD negativity rates • Sarclisa-Kd associated with severe respiratory infections

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Important Considerations for Use of Monoclonal Antibodies

Darzalex

- **Infusion reactions**
  - Less with SC use
- Risk of **shingles**
  - Use appropriate vaccination
- Increased risk of **hypogammaglobulinemia** and upper respiratory infections
  - Bactrim prophylaxis
  - IVIG support

Empliciti

- **Infusion reactions**
- Risk of **shingles**
  - Use appropriate vaccination

Sarclisa

- **Infusion reactions**
- Risk of **shingles**
  - Use appropriate vaccination

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Treatment Approach

First relapse

Proteasome inhibitor (PI)/ immunomodulatory drug (IMiD)/ antibody-based therapy

>1 Relapse

Any options for first relapse not tried

- Refractory to Velcade ***and*** Revlimid → DKd, Isa-Kd, DPd, Elo-Pd, Isa-Pd, or KPd
- Refractory to an IMiD, but sensitive to a PI → DVd, SVd, Ven-Vd (for t[11;14])*

or

Triple-class refractory

- Approved therapies → Sd, Abecma, Carvykti, Tecvayli
- Clinical trials → Bispecific/ trispecific antibodies, CAR T cells, CELMoDs

D, daratumumab (Darzalex); K, carfilzomib (Kyprolis); d, dexamethasone; Isa, isatuximab (Sarclisa); P, pomalidomide (Pomalyst); Elo, elotuzumab (Empliciti); V, bortezomib (Velcade); S, selinexor (Xpovio); Ven, venetoclax (Venclexta)

*Not yet approved for use in myeloma patients.

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Triple-Class Refractory

- For patients with relapsed or refractory multiple myeloma who have received treatment with—and did not respond satisfactorily to, or progressed while on treatment with—the three main classes of drugs currently used to treat myeloma are...

Proteasome inhibitors	Immunomodulatory drugs	Anti-CD38 monoclonal antibodies
• Velcade (bortezomib) • Kyprolis (carfilzomib) • Ninlaro (ixazomib)	• Revlimid (lenalidomide) • Pomalyst (pomalidomide)	• Darzalex (daratumumab) • Sarclisa (isatuximab)

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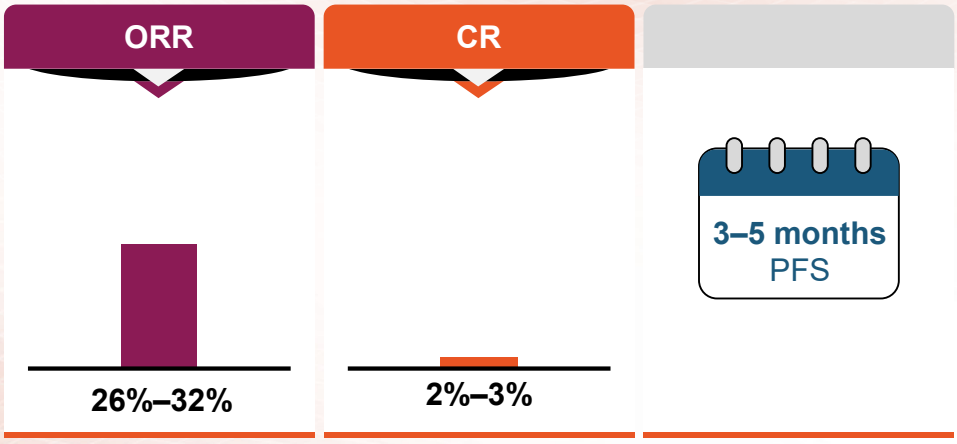
Where We've Been: Outcomes for Later-Line Triple Class-Exposed Patients With RRMM



Exposed to an immunomodulatory imide drug, proteasome inhibitor, and CD38 monoclonal antibody
Gandhi UH et al. *Leukemia*. 2019;33(9):2266.

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Currently Available Drugs for Triple-Class Refractory Myeloma

Class	Drug	Formulation		Approval
Nuclear export inhibitor	XPOVIO (selinexor)		Twice-weekly pill	• For **relapsed/refractory** myeloma in combination with dexamethasone (after at least 4 prior therapies and whose disease is refractory to at least 2 PIs, at least 2 IMiDs, and an anti-CD38 mAb
Chimeric antigen receptor (CAR) T cell	Abecma (idecabtagene vicleucel)*		300 to 460 × 10^6 genetically modified autologous CAR T cells in one or more infusion bags	• For **relapsed/refractory** myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb
CAR T cell	Carvykti (ciltacabtagene autoleucel)†		0.5 to 1.0 × 10^6 genetically modified autologous CAR T cells/kg of body weight	• For **relapsed/refractory** myeloma (after 4 or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb
Bispecific antibody	Tecvayli (teclistamab)‡		Step-up dosing§ the first week then once weekly thereafter by subcutaneous injection	• For **relapsed/ refractory** myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)

IMiD, immunomodulatory agent; PI, proteasome inhibitor; mAb, monoclonal antibody

*Black box warning: cytokine release syndrome; neurologic toxicities; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia

†Black box warning: cytokine release syndrome; neurologic toxicities; Parkinsonism and Guillain-Barré syndrome; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia
Abecma and Carvykti are available only through a restricted distribution program

‡Black box warning: cytokine release syndrome; neurologic toxicities.

†Patients are hospitalized for 48 hours after administration of all step-up doses.

§Tecvayli is available only through a restricted distribution program.

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XPOVIO + Dexamethasone in Relapsed/Refractory Myeloma

	No. patients with ≥PR (%)[1]
Total	32 (26)
Previous therapies to which the disease was refractory, n (%)	
Velcade, Kyprolis, Revlimid, Pomalyst, and Darzalex	21 (25)
Kyprolis, Revlimid, Pomalyst, and Darzalex	26 (26)
Velcade, Kyprolis, Pomalyst, and Darzalex	25 (27)
Kyprolis, Pomalyst, and Darzalex	31 (26)

Additional analyses showed clinical benefit with XPOVIO regardless of patient age and kidney function.[2,3]

1. STORM Trial. Chari A et al. *N Engl J Med*. 2019;381:727. **2.** Gavriatopoulou M et al. Presented at the 17th International Myeloma Workshop; September 12-15, 2019. Abstract FP-110. **3.** Vogl DT et al. Presented at the 17th International Myeloma Workshop; September 12-15, 2019. Abstract FP-111.

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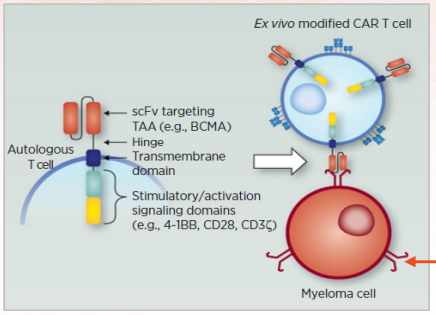
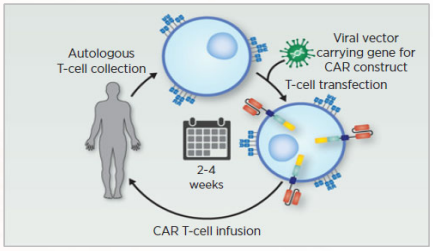
CAR T-Cell Therapy

- Genetically modified T cells designed to recognize specific proteins on MM cells
- CAR T cells are activated once in contact with the MM cell and can destroy the MM cell
- CAR T cells can persist for long periods of time in the body
- CAR T cells are created from a patient's own blood cells, but the technology is evolving to develop "off-the-shelf" varieties



B-cell maturation antigen (BCMA)



Examples:
- Abecma (ide-cel)
- Carvykti (cilta-cel)
- CT103A
- Gamma secretase inhibitor followed by CAR T-cells

CAR, chimeric antigen receptor; MM, multiple myeloma
Cohen A et al. *Clin Cancer Res.* 2020;26:1541.

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CAR T-Cell Therapy Patient Journey

Apheresis 1	**1 day**	**Immune cells from the patient are collected**
(Manufacturing) Patients return home 2	**4–6 weeks**	**Standard of care therapy is permitted until CAR T cells are ready for infusion**
Lymphodepletion (chemotherapy) 3	**3 days**	**Fludarabine and Cytoxan are used to create "immunologic space" to CAR T cells to expand**
Infusion 4	**2 weeks**	
Follow up 5	**Within 2 weeks**	

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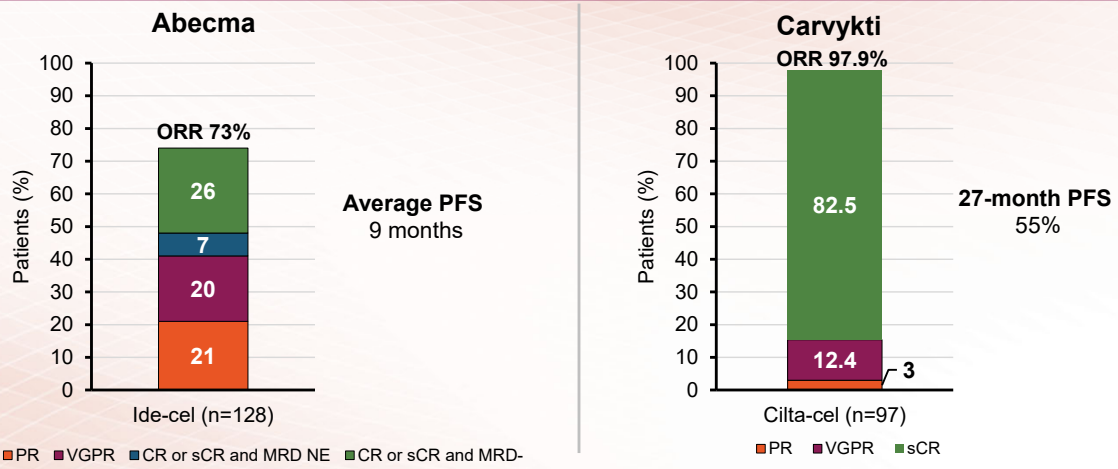
Two CAR T-Cell Therapies Approved!



ORR, overall response rate; PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response; MRD, minimal residual disease; PFS, progression-free survival

KarMMa Trial. Munshi NC et al. *N Engl J Med*. 2021;384:705.
CARTITUDE-1 Trial. Berdeja JG et al. *Lancet*. 2021;398:314; Martin T et al. *J Clin Oncol*. June 4, 2022 [Epub ahead of print].

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CAR T: Expected Toxicities

Cytokine release syndrome (CRS)

Neurotoxicity (ICANS)

Cytopenias

Infections

	CRS	ICANS
Onset	1–9 days after CAR T-cell infusion	2–9 days after CAR T-cell infusion
Duration	5–11 days	3–17 days
Symptoms	• Fever • Difficulty breathing • Dizziness • Nausea • Headache • Rapid heartbeat • Low blood pressure	• Headache • Confusion • Language disturbance • Seizures • Delirium • Cerebral edema
Management	• Actemra (tocilizumab) • Corticosteroids • Supportive care	• Antiseizure medications • Corticosteroids

*Based on the ASTCT consensus; †Based on vasopressor; ‡For adults and children >12 years; §For children ≤12 years; ǂOnly when concurrent with CRS

Xiao X et al. *J Exp Clin Cancer Res*. 2021;40(1):367. Lee DW et al. *Biol Blood Marrow Transplant*. 2019;25:625;
Shah N et al. *J Immunother Cancer*. 2020;8:e000734.

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Transplant vs CAR T Cells

Cellular therapies	CAR T-cell therapy	Autologous stem cell transplantation
Patient's cells collected	Yes	Yes
Types of cells collected	T cells*	Stem cells†
Collected cells are genetically engineered in a lab	Yes	No
Patient given chemotherapy before cells are infused back into patient	Yes, lymphodepleting therapy	Yes, melphalan
When in the course of myeloma is this *usually* done?	After multiple relapses	As part of initial treatment
Side effects of treatment	Cytokine release syndrome; confusion	Fatigue, nausea, diarrhea

*An immune cell that is the "business end" of the system, in charge of maintaining order and removing cells.
†Precursor cells that give rise to many types of blood cells. We actually collect CD34+ve cells.

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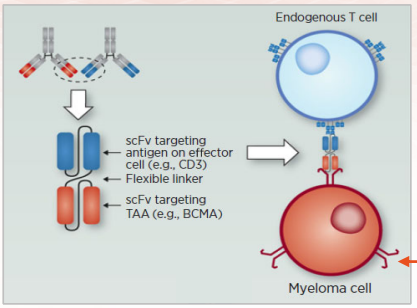
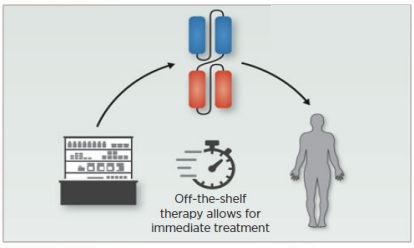
Bispecific Antibodies

- Bispecific antibodies are also referred to as *dual specific antibodies, bifunctional antibodies,* or *T-cell engaging antibodies*
- Bispecific antibodies can target two cell surface molecules at the same time (one on the myeloma cell and one on a T cell)
- Many different bispecific antibodies are in clinical development; none are approved for use in myeloma
- Availability is off-the-shelf, allowing for immediate treatment



BCMA, GPRC5D, or FcRH5



Examples:
- Elranatamab
- Teclistamab
- TNB-303B (ABBV-383)
- REGN5458
- Cevostamab
- Talquetamab

Cohen A et al. *Clin Cancer Res.* 2020;26:1541.

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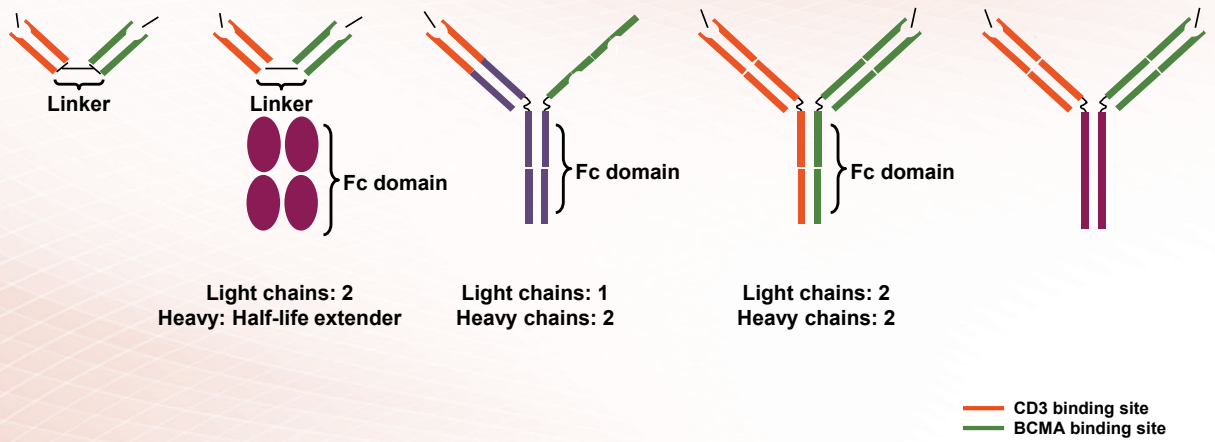
There Are Different Types of Bispecific T-Cell Engagers/Antibodies



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Bispecific Antibodies: >20% Activity

Myeloma cell target	Bispecific agent	Patients responding*
BCMA	Teclistamab	63%
BCMA	REGN5458	73%
BCMA	Elranatamab	73%
BCMA	TNB383B	60%
BCMA	CC93269	89%
BCMA	AMG701	83%
GPRC5D	Talquetamab	70%
FCRH5	Cevostamab	55%

*Based on a recent sampling

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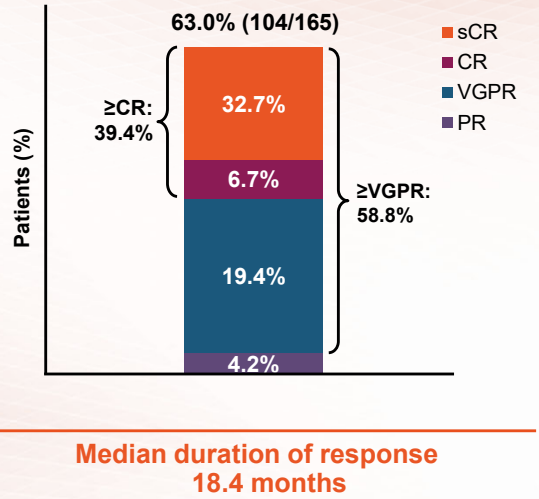
Now Approved: Tecvayli, the First Bispecific Antibody



Median duration of response
18.4 months

Moreau P et al. *N Engl J Med*. 2022;387:495.

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Bispecific Antibodies: Expected Toxicities

- Cytokine release syndrome (CRS)
- Neurotoxicity (ICANS)
  - Usually occurs within first 1–2 weeks
  - Frequency (all grade and grade 3–5) higher with CAR T
- Cytopenias
- Target unique
  - For example, rash, taste disturbance seen with GPRC5D, but not with BCMA
- Infections
  - Incidence for bispecifics at RP2D not yet known
  - Viruses: CMV, EBV
  - PCP/PJP
  - Ongoing discussions regarding prophylactic measures
    - IVIG
    - Anti-infectives

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BCMA-Targeted Therapies Are Associated With an Increased Risk of Infections

- Both viral and bacterial
  - Up to 1/3 of patients in clinical trials have serious infections (requiring IV antibodies or hospitalization)
- Increased risk of serious COVID complications despite history of vaccination
  - Antibody levels
  - Tixagevimab co-packaged with cilgavimab (EVUSHELD)
  - Immediate treatment once diagnosed nirmatrelvir with ritonavir (Paxlovid)
    - Start as soon as possible; must begin within 5 days of when symptoms start

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Similarities and Differences Between CAR T-Cell Therapy and Bispecific Antibodies

	CAR T-cell therapy	Bispecific antibody
Approved product	Abecma, Carvykti	Tecvayli
Efficacy	++++	+++
How given	One-and-done	IV or SC, weekly to every 3 weeks until progression
Where given	Academic medical centers	Academic medical centers
Notable adverse events	CRS and neurotoxicity	CRS and neurotoxicity
Cytokine release syndrome	+++	++
Neurotoxicity	++	+
Availability	Wait time for manufacturing	Off-the-shelf, close monitoring for CRS and neurotoxicity

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Options on the Horizon

Clinical phase	Novel agents		Immunotherapies					
	Precision medicine	Novel mechanisms of action†	Immuno-modulatory agents	Naked antibodies†	Antibody-drug conjugates	Bispecific antibodies and bispecific T-cell engagers†	CAR T-cell therapies†	Checkpoint inhibitors
Phase 3	Venetoclax*		Iberdomide			Talquetamab		
Phase 1, 2	Abemaciclib* Cobimetinib* Dabrafenib Enasidenib* Erdafitinib* Idasanutlin Trametinib Vemurafenib	ABBV-43 AMG-176 AMG-232 APG-2575 Azacitidine BGB-11417 BMF-219 CFT7455 Citarinostat COM902 CYT-0851 Disulfiram Duvelisib	Avadomide Mezigdomide Modakafusp alfa	AB308 ALT-803 AO-176 BMS-986207 EOS884448 Feladilimab GEN3014 GSK3174998 Lirilumab Magrolimab	AMG-224 CC-99712 FOR46 HDP-101 MED12228 MT-0169 STI-6129 STRO-001	AMG 701 Cevostamab CC-92328 CC-93269 CC-95266 Elranatamab HPN217 ISB 1342 REGN5458 REGN5459 TNB-383B	ALLO-605 ALLO-715 ATLCAR.CD138 CART-ddBCMA CART-TnMUC1 CC-98633 CS1-CART CTX120 CYAD-211	Abatacept Cemiplimab Dostarlimab Durvalumab Ipilimumab Nivolumab Pembrolizumab TTI-622 Zimberelimab

*Being studied in the MyDRUG trial; †More agents can be found at www.clinicaltrials.gov

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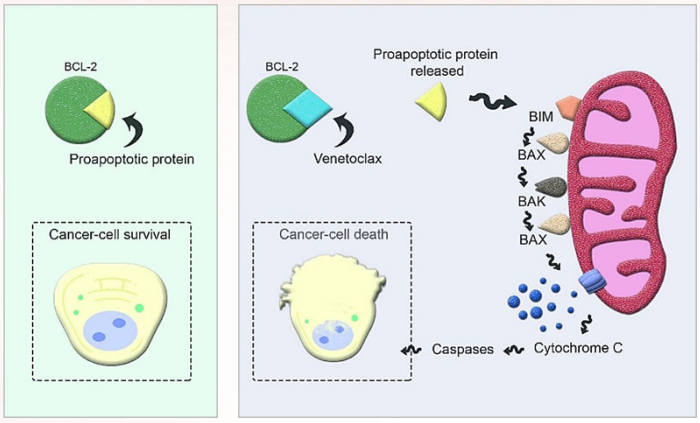
Venetoclax and t(11;14)

Venetoclax is a Bcl-2 inhibitor

- BCL2 inhibitor
- Induces cancer cell death
- t(11;14) multiple myeloma → ↑BCL2 and ↓MCL1
- t(11;14): first predictive marker in multiple myeloma, indicating susceptibility to BCL2 inhibition



Ehsan H et al. *J Hematol.* 2021;10:89.

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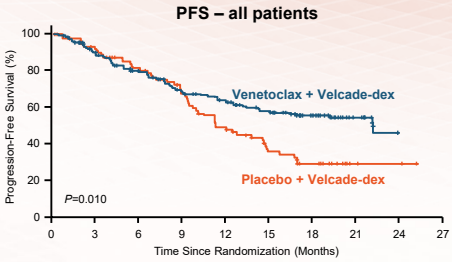
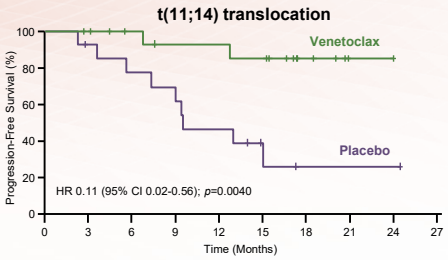
Venetoclax and t(11;14)

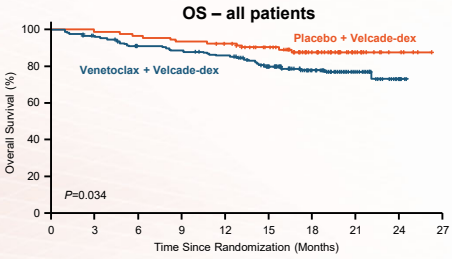
Venetoclax bortezomib dex vs placebo bortezomib dex;
1–3 prior lines

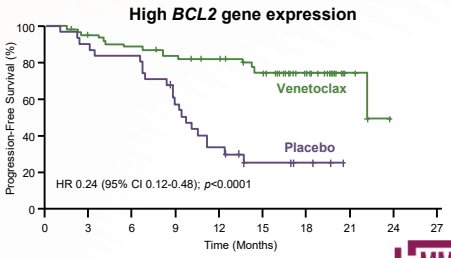
Median follow up 18.7 m mPFS
22.4 m venetoclax
11.5 m placebo

Venetoclax especially active in t(11;14) or *BCL2*^{high} MM









The BELLINI Trial. Kumar SK et al. *Lancet Oncol*. 2020;21:1630.

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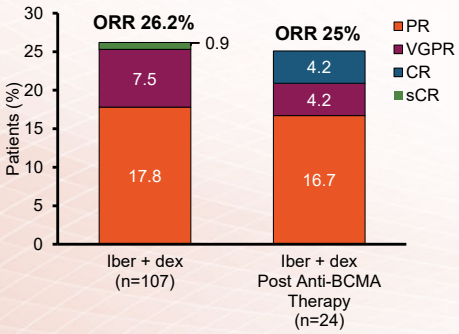
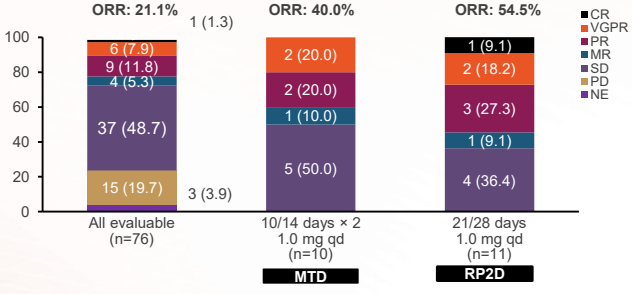
Cereblon E3 Ligase Modulators (CELMoDs)

CELMoDs are related to the immunomodulatory drugs (IMiDs) but are more potent and may overcome resistance to IMiDs

Iberdomide in combination with dexamethasone in patients with relapsed/refractory multiple myeloma[1]



Mezigdomide in combination with dexamethasone in patients with relapsed/refractory multiple myeloma[2]



1. Lonial S et al. *Blood*. 2021;138. Abstract 162; 2. Richardson PG et al. *J Clin Oncol*. 2020;38. Abstract 8500

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Summary

- We now have many different options for relapsed myeloma depending on patient and myeloma factors at relapse.
- Therapy choices will depend on teamwork between physician, patient, and caregivers and are based on many decision points.
- Combinations of proteasome inhibitors with either immunomodulatory drugs or selinexor improve progression-free survival.
- We have three different monoclonal antibodies that improve progression-free survival when added to other standard therapies without significantly increasing side effects.
- Abecma and Carvykti are only the first-generation CAR T cells and target the same protein. Different CAR Ts and different targets are on the way.
- Bispecific antibodies represent an "off-the-shelf" immunotherapy; Tecvayli was approved in October 2022. Several additional bispecific antibodies are under clinical evaluation..
- Many other exciting options are in trials and look very promising.

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Please take a moment to answer two questions about this presentation.

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MULTIPLE MYELOMA Research Foundation

Health Care Disparities in Multiple Myeloma

Laura Finn, MD, MS
Ochsner Health
New Orleans, Louisiana

Yvens Laborde, MD
Ochsner Health
New Orleans, Louisiana

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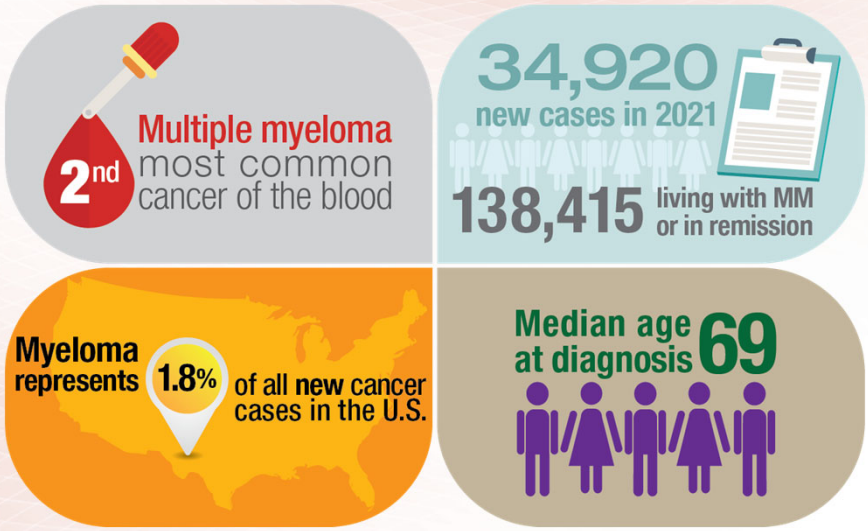
How common is multiple myeloma?



SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/mulmy.html

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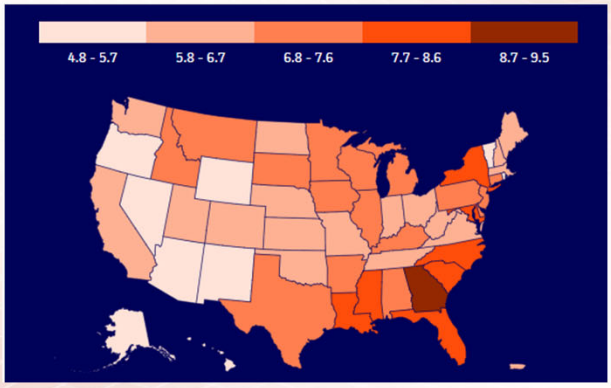
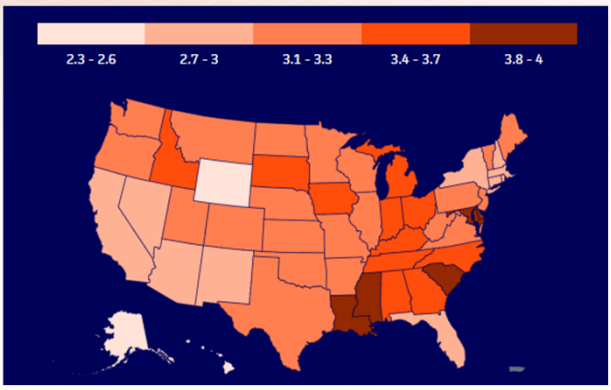
Incidence rates, 2014–2018
Myeloma, by state



Average annual rate per 100,000, age adjusted to the 2000 US standard population.

Data sources: North American Association of Central Cancer Registries (NAACCR), 2021

Death rates, 2015–2019
Myeloma, by state



Average annual rate per 100,000, age adjusted to the 2000 US standard population.

Data sources: National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, 2021

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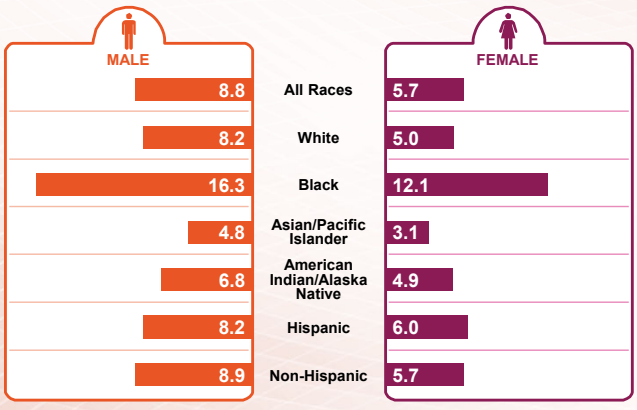
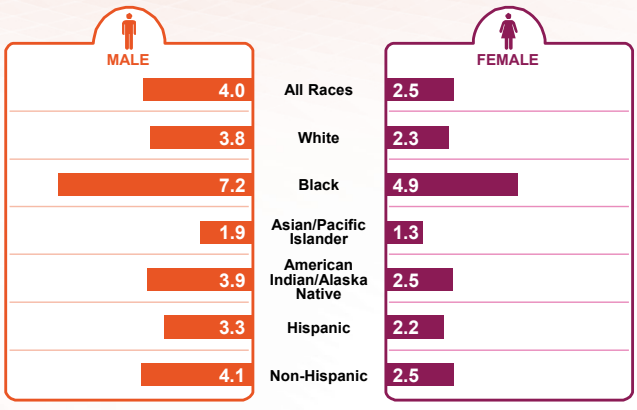
Multiple Myeloma Is Twice as Common in Black Patients

Rate of new cases per 100,000 persons by race/ethnicity and sex



SEER 21 20144-2018, Age-Adjusted

Death rate per 100,000 persons by race/ethnicity and sex



U.S. 2015-2019, Age-Adjusted

SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/mulmy.html

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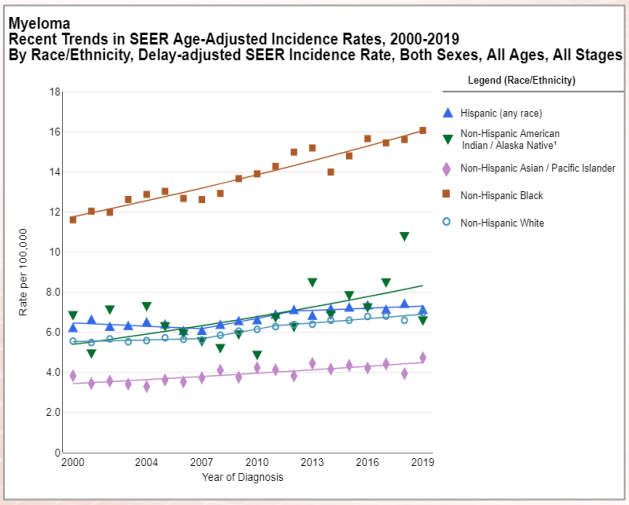
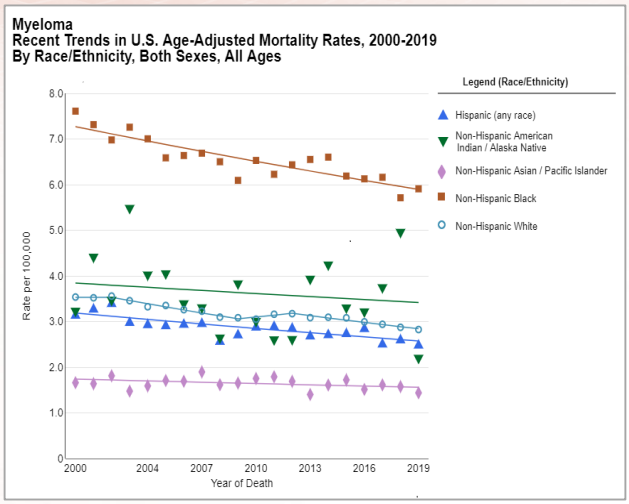
Multiple Myeloma Incidence and Mortality by Race/Ethnicity





SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD. https://seer.cancer.gov/statistics-network/explorer/application.html

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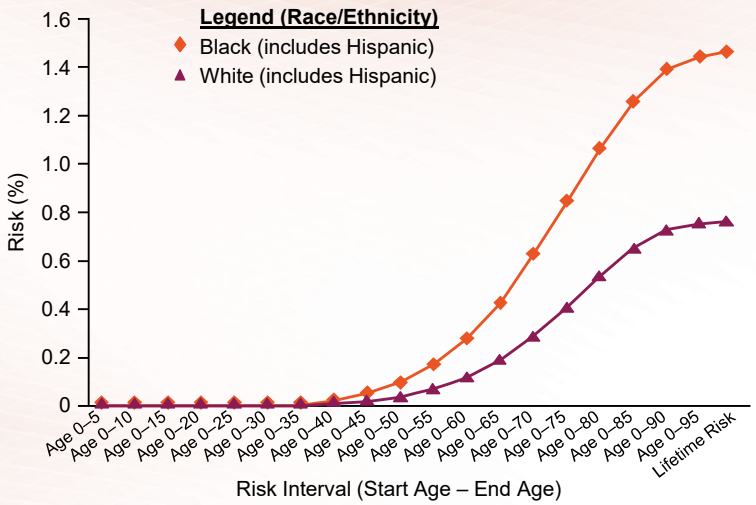
Risk of Myeloma Diagnosis by Age

Black patients are diagnosed at an earlier age and have a twofold risk of being diagnosed with multiple myeloma



Data from National Cancer Institute
Surveillance, Epidemiology, and End Results Program (SEER)

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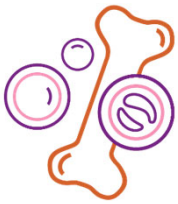
Multiple Myeloma in Black Patients

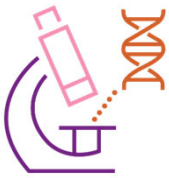
Demographics

- ↑ Myeloma prevalence (2× White patients)[1]
- Older adults have ↑ prevalence of the myeloma precursor condition MGUS[2]
- Younger[3-5]



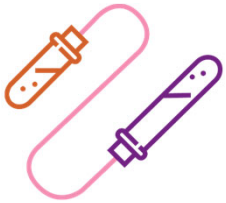
Clinical factors

- ↑ Comorbidities[3,6]
- ↑ Incidence of all myeloma-defining events (for example, hypercalcemia, renal dysfunction, anemia, dialysis) **except bone fractures**[7]



Molecular (genetic) factors

- Significant differences in the frequency of certain chromosomal abnormalities:
  - High risk cytogenetics including del17p are seen **less frequently**[8]
  - Some other mutations seen more frequently but significance not known[9]



Treatment

- Significantly lower stem cell transplant utilization[7,9-13]

1. SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD. http://seer.cancer.gov/statfacts/html/mulmy.html. **2.** El-Khoury H et al. *Blood*. 2021;138. Abstract 152. **3.** Blue B et al. *Br J Haematol*. 2017;176:322. **4.** Waxman AJ et al. *Blood*. 2010;116:5501. **5.** Ailawadhi S et al. *Blood Cancer J*. 2018;8:67. **6.** Schoen MW et al. *Blood*. 2019;134. Abstract 383. **7.** Ailawadhi S et al. *Cancer*. 2018;124:1710. **8.** Baker A et al. *Blood*. 2013;121:3147. **9.** Manojilovic Z et al. *PLoS Genet*. 2017;13:e1007087. **10.** Ailawadhi S et al. *Cancer Med*. 2017;6:2876. **11.** Fiala M et al. *Cancer*. 2017;123:1590. **12.** Costa LJ et al. *Biol Blood Marrow Transplant*. 2015;21:701. **13.** Vardell VA et al. *Blood*. 2019;134. Abstract 423.

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Disparities in Care in Black Patients

- Several studies have shown that the use of standard therapies tends to be significantly lower in Black patients
- However, with equal access to standard therapy, the outcome in Black patients is equal or superior to that of White patients

Treatment type	Use in Black patients	Use in White patients	*P* value
Triplet therapy	**47%**	61%	0.004
Stem cell transplantation	**30%**	40%	0.034

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Reasons for Disparities in Outcomes for Black Americans With Multiple Myeloma and Other Cancers

- Less access to cancer screening services
- Structural racism
- Social determinants of health
- Shortage of African American physicians and lack of familiarity with black economic and social conditions
- Comorbid conditions
- Delayed onset of diagnosis and severity of disease at the time of diagnosis
- Lack of access to the same level of treatment as White patients
- Low enrollment in clinical trials

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Key Points

Despite disparities in incidence and outcomes of multiple myeloma among Black patients, evidence suggests that these disparities can be overcome:

- ✓ **Ensure equal access to appropriate therapeutic options for Black patients**
- ✓ **Increase awareness of these disparities and their solutions to patients, physicians, and the communities**

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Please take a moment to answer two questions about this presentation.

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MULTIPLE MYELOMA
Research Foundation

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MULTIPLE MYELOMA Research Foundation

Patient Experience

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Town Hall Questions & Answers

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Thank you!

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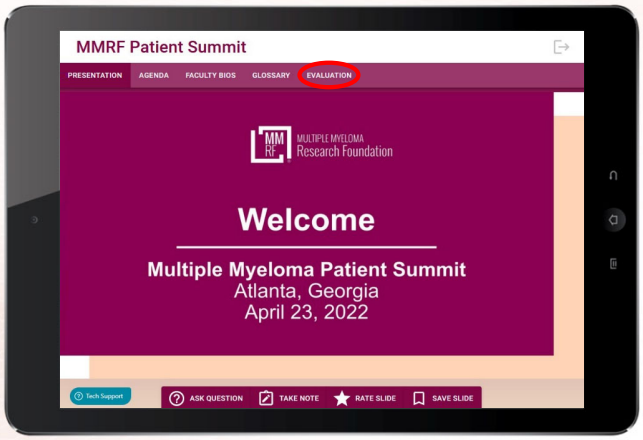
Don't Forget!

Complete your evaluation
Leave the iPad at your seat



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Upcoming Patient Education Events
Save the Date

Topic	Date and Time	Speakers
Facebook Live Session—Relapsed/Refractory Multiple Myeloma	Thursday, December 15 4:00 PM – 5:00 PM (ET)	Nitya Nathwani, MD
Expert Session: Multiple Myeloma Highlights From the 2022 American Society of Hematology Meeting	Tuesday, December 20 1:00 PM – 3:00 PM (ET)	Hearn Jay Cho, MD, PhD Joshua Richter, MD

For more information or to register,
please visit themmrf.org/resources/education-program

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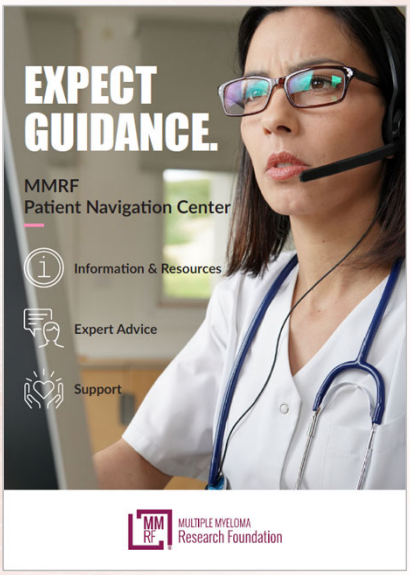
MMRF Patient Resources



MMRF Patient Navigation Center

You and your care team will have many decisions to make along your treatment journey. The Patient Navigation Center is a space for multiple myeloma patients and their caregivers to connect with patient navigators — who are professionals specializing in oncology — for guidance, information, and support. You can connect with a patient navigator via phone, or email. Whatever questions you may have, our patient navigators are here to help.

MMRF Patient Navigators include:
- Grace Allison, RN, BSN, OCN, RN-BC
- Brittany Hartmann, RN-BSN
- Erin Mensching, RN-BSN, OCN

THE RIGHT TRACK

Get on the right track for you

The MMRF's Right Track program puts you on the path to the best results for you.

Right Team
Access experts and centers that have extensive experience treating multiple myeloma.

Right Tests
Get the information, tests, and precise diagnoses to make the right treatment decisions.

Right Treatment
Work with your team to consider the best treatment plan and identify clinical trials that are right for you.

Contact the Patient Navigation Center Today

Looking for guidance? We're here to help.

Monday – Friday | 9:00AM – 7:00PM ET

Phone: 1-888-841-MMRF (6673) Online: TheMMRF.org/PatientNavigationCenter

Email: patientnavigator@themmrf.org

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Myeloma Mentors®

Myeloma Mentors® allows patients and caregivers the opportunity to connect with trained mentors. This is a phone-based program offering an opportunity for a patient and/or caregiver to connect one-on-one with a trained patient and/or caregiver mentor to share his or her patient journeys and experiences.

No matter what your disease state—smoldering, newly diagnosed, or relapsed/refractory—our mentors have insights and information that can be beneficial to both patients and their caregivers.

Contact the Patient Navigation Center at 888-841-6673 to be connected to a Myeloma Mentor or to learn more.

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A Cure Is Within Reach
Join the myeloma community from around the world as a member of the MMRF Team for Cures and become an integral part of the team, accelerating a cure for each and every patient! The MMRF is determined to make multiple myeloma curable, and we will stop at nothing to reach that goal.
Find your event today!
theMMRF.org/Events
5K Walk/Run
Taking steps to cure cancer
Join one of 15 MMRF Team for Cures 5K Walk/Runs across the country or from anywhere in the world as a virtual participant! Participation brings the myeloma community together for camaraderie and knowledge sharing in a family-friendly fundraising event.
theMMRF.org/5K
Current Walk/Run Events
South Florida • Scottsdale • San Francisco • Boston • Atlanta
Dallas • Southeast Michigan • Connecticut • Charlotte
Chicago • Twin Cities • Washington, DC • Philadelphia
New York City • Los Angeles
Marathons & Half-Marathons
Crossing a finish line for a cure
Since 2007, over 2,700 athletes have raised more than $13.6 million to accelerate a cure for multiple myeloma. We offer entry to some of the top marathons and half marathons in the world, including five of the six Abbott World Marathon Majors.
theMMRF.org/Marathon
Current Marathons and Half-Marathons
United Airlines NYC Half Marathon • Boston Marathon
BMW Berlin Marathon • Virgin Money London Marathon
Bank of America Chicago Marathon • TCS New York City Marathon
Today I RAN for a CURE!
Moving Mountains for Multiple Myeloma
Reach new heights, accelerate cures
Myeloma patients, doctors, nurses, and other caregivers have been taking on epic peaks across the globe for this program since 2016. Each trek emphasizes the collaboration necessary to drive toward cures and the incredible feats that can be accomplished when the myeloma community comes together to raise critical funds.
theMMRF.org/Hike
Current and Past Treks
Mount Kilimanjaro • Grand Canyon • Machu Picchu
Mount Fuji • Everest Base Camp • Mount Washington
Sweden • Colorado • Greenland • Patagonia • Iceland
Road to Victories
Achieving victories over cancer
These inspirational cross-country rides take cyclists on epic journeys on multiple continents, all to raise critical funds to fight myeloma. Patients, caregivers, doctors, and pharma partners have conquered over 3,400 miles and counting for this incredible cycling program.
RoadtoVictories.com
Current and Past Rides
Vermont to Quebec • London to Paris • Glacier National Park
Bryce Canyon and Zion National Park • The Coast of Maine

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